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Book Reviews

Particle Adhesion: Applications and Advances. David J. Quesnel, Donald S. Rimai, and Louis H. Sharpe, Eds. Taylor & Francis, New York, NY. www.tandf.co.uk. 2001. 504 pp. $80.00.

Particle adhesion is an important phenomenon in a number of fields not least of which are pharmaceutical research and development. This volume acts as a guide to a variety of areas in which an understanding of adhesion is valuable. The chapters were selected from papers presented at the *Particle Division Symposia of the 22nd and 23rd Annual Meetings of the Adhesion Society*. The preface adequately introduces each of the sections of the book and pre-emptively links then in a sequential manner. Indeed, the outline makes the reviewer's task simpler as the editors have given a concise overview of each of the author's contributions. The book is divided into six sections describing particle adhesion in biology; rheology (elastic and viscoelastic effects); surface interactions; conductivity; single-particle experiments and control. There are a total of 21 chapters unevenly distributed between the major topics. The majority of chapters appear in the biology section, and there is a single chapter describing electrical conductivity through particles.

Love and Fursten initiate the discussion of particle adhesion in biology with a perspective on metastasis. These authors apply first principles of particle interaction in the form of Derjagnin and Landau and Vervey and Overbeek (DLVO) and Johnson, Kendall, and Robert (JKR) theories to cadherins, and the process of metastasis of cancer cells. The overall objective is to explain cell detachment in physicochemical terms, but the approach is complicated by population considerations relative to individual cell-cell interactions. Moss and Anderson take and alternative view of cancer cells, hoping to elucidate adhesion to endothelial monolayers. These authors describe cell culture experiments aimed at quantifying the numbers of cells attaching and the resistance to detachment at certain applied shear stresses. Attenborough and Kendall turn their attention to cell-cell adhesion of erythrocytes. A variety of physicochemical methods for viewing detachment are described including direct visualization and electrical resistance particle size determinations to estimate aggregation. Carter and colleagues study the dependence of phagocytosis on particle composition. The context of this work is inflammatory response to implant wear debris. The degradable nature of particles appeared to influence phagocystosis, inflammation, and thereby severe osseous destruction. Baier *et al.* continue the theme of phagocytic responses by considering large substrata vs. small particle. A variety of inflammatory outcomes were measured including cell viability, endotoxin testing, production of reactive oxygen intermediates, and cell morphological characteristics. The response of monocyte-derived macrophages was dependent on large unbroken substrate surfaces rather than the type of particles contacted during the first hour of exposure. In a subsequent chapter, Baier and co-workers examined the influence of particle shape on lung tissue responses following inhalation. These particles were viewed as inadvertent implants.

The rheological section begins with a contribution from Reisema, Biggs, and Craig focusing on the specific measurement of the adhesion of a viscoelastic sphere to a flat noncompliant surface using atomic force microscopy (AFM) to examine the adhesion between a single polystyrene bead and a flat silica surface. Quesnel and Rimai introduce a theoretical approach of finite element modeling of particle adhesion to derive a formal expression for surface energy. Unertl describes creep effects in nanometer-scale contacts to viscoelastic materials. Guidelines for selection of optimal experimental parameters for nanometer-scale studies are presented, and the need for a comprehensive theory is emphasized. Rheological properties are a physical manifestation of particle-particle and particle-surface interactions, which are the subject of the next section of the book. Brach, Dunn, and Li describe the impact of microparticles on solid surfaces. A large number of experiments are summarized, and analytical models of the impact process are described.

A series of papers then appear examining different particle detachment phenomena and structural features. Rimai and colleagues studied the adhesion of irregularly shaped, 8-μm-diameter particles to substrates. An ultracentrifuge was employed to study the removal of irregularly shaped polyester particles from a polyester substrate. In addition, detachment of nanometer silica clusters was evaluated. Ultimately, the contributions of electrostatic and van der Waals interactions were assessed. Marshall describes a new conductive resin composed of copper-based polymer systems. Taikka and co-workers describe interactions between micrometer-sized glass particles and poly(dimethyl siloxane) in the absence and presence of applied loads.

Unique methods are required to evaluate surface adhesion properties. Shaeffer and Gomez describe the use of atomic force microscopy in jump mode with respect to cantilever probing of the surface to obtain adhesion maps. Drelich *et al.* use AFM to measure adhesion forces between polyethylene particles and mineral substrates in aqueous solutions of ethoxylate alcohols. Dickinson, Hariadi, and Langford use scanning probe microscopy to detach nanometer-scale, single-crystal sodium chloride particle grown on soda-lime glass substrates. In two papers, Busnaina and colleagues describe the effects of environmental conditions, namely relative humidity, on particle adhesion. The effect of high humidity is to increase capillary forces, which contribute to adhesion, and this is a time-dependent phenomenon. The conclusion of the book deals with theoretical models that are not integrated as tightly with the foregoing chapters. Prisman describes the theory of nonequilibrium deposition of submicrometer particles. Zhang and Ahmadi bring the book to its conclusion by describing aerosol particle removal and re-entrainment in turbulent channel flows using a numerical simulation approach.

This is a detailed text examining situations in which particle adhesion plays a fundamental role and describing analytical and experimental approaches to addressing these phenomena. There are numerous figures, tables, and references and a good balance of theory and practice. The direct application of some of the techniques described in pharmaceutical analysis has already occurred. AFM has frequently been used

in the past decade to evaluate surface properties of excipient and drug particles. However, other approaches are described, which might well be useful in a therapeutic context. Each of the authors should be commended for their contributions and the editors for their vision in structuring the book to achieve a theme from such diverse topics. Anyone concerned with the nature of particle adhesion from tissue engineering to pharmaceutical technology and product development will find this book stimulating reading and a good reference text. I am pleased to have it join other particle science volumes on my bookshelf.

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Drug Delivery Systems. Second Edn. Vasant V. Ranade and Mannfred A. Hollinger. (Pharmacology & Toxicology Series). CRC Press, Boca Raton, FL. www.crcpress.com. 2004. 448 pp. $179.95.

The second edition of this book in the very popular CRC Press series on Pharmacology and Toxicology serves as an excellent review source on current information on drug delivery systems. It is divided into five sections: site-specific drug delivery; polymers, implantable drug delivery; oral drug delivery; transdermal, intranasal, ocular, and miscellaneous drug delivery; and regulatory considerations and global outlook. The book is well organized in that each chapter provides the reader with a table of products marketed and currently under investigation that is useful to the reader. In addition, sections on "Recent Advances" are added at the end of each chapter, which outline key areas as well as provide updates on the newest products on the market.

The first chapter deals with liposomes, the basic background and liposomes as drug carriers. There is a useful well-referenced section toward the end of the chapter where the authors use a bulleted list to cover highlights of current research. In Chapter 2, monoclonal antibodies and their particular use in site-specific drug delivery are discussed. Their production and scale-up are briefly covered as well as *in vitro* and *in vivo* testing. Several pages are devoted to updates on the monoclonal antibody research covering a wide range of data. Examples include less conventional approaches of human monoclonal antibody production using gene cloning strategies that will allow the possibility of much more sophisticated targeting for novel therapies. Chapter 3 reviews roles of polymers in drug delivery and elegantly divides the subject into classes of currently available polymeric materials (diffusion controlled, solvent activated, chemically controlled, and magnetically controlled systems) followed by a review of soluble polymers, biodegradable/bioerodible polymers, mucoadhesive, polymers containing pendant bioactive substituents, matrix systems, heparin-releasing polymers, ionic polymers, oligomers, and a section on miscellaneous and recent advances. Chapter 4 focuses mainly on insulin and implants for contraception. Chemotherapeutic agents and cancer pain management using implants were briefly discussed.

Oral drug delivery is reviewed in Chapter 5. The topic is divided into basic background on the GI tract, targeting of drugs, and mathematical modeling. The authors then present the design and fabrication of controlled-release devices. The topics discussed are dissolution-, diffusion-, osmotically, and chemically controlled release approaches followed by a fairly extensive discussion covering over 16 miscellaneous forms for oral drug delivery. Recent advances in the area are covered by bulleted sections of a paragraph length with references, allowing the readers to go to the original papers and reviews, if necessary. An extensive table provides a listing of products under development with the names of the developers. Chapter 6 focuses on transdermal drug delivery and touches upon development of transdermal systems and methods of enhancing drug permeation through the skin as exemplified by iontophoresis. The next two chapters cover nasal and ocular as well as miscellaneous forms of drug delivery. Chapters 9 and 10 present a broad overview on regulatory considerations of drug delivery systems and the global outlook of the drug delivery industry.

This book has been successful in condensing a large volume of information that would require several volumes of this size for thorough review. The authors covered in some depth most of the important areas with extensive references that the readers can use for further detailed information. This book belongs on the shelves of pharmaceutical scientists as a short reference guide to the discipline. Students will also find this text useful for surveying the broad topic of drug delivery systems in a relatively small volume. The downside with this book is that no topic is covered in great depth and, as most books suffer from, the bibliography is not totally up to date in an area that is moving forward at a rapid pace.

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Modified-Release Drug Delivery Technology. Michael J. Rathbone, Jonathan Hadgraft, and Michael S, Roberts, Eds. (Drugs and the Pharmaceutical Sciences, Vol. 126). Marcel Dekker, New York, NY. www.dekker.com. 2003. 996 pp. $195.00.

The field of controlled drug delivery technologies is more than five decades old. The keyword search of drug delivery in the Sci-Finder Scholar database resulted in more than 100,000 references. Of these, about 300 references are books. These books collectively cover all aspects of controlled drug delivery. Most of the books, however, cover only certain aspects of drug delivery technologies, and no individual book presents comprehensive information on the subject. Once in a while we are fortunate enough to find a single volume that summarizes all the work done from the past to the time of publication of the book. The first comprehensive book on drug de-

livery technology is *Sustained and Controlled Release Drug Delivery Systems*, edited by Joseph R. Robinson and published in 1978. This book describes the fundamentals of controlled drug delivery technologies. The next comprehensive book is probably *Novel Drug Delivery Systems*, edited by Yie W. Chien in 1992. One of the main thrusts of this book is mathematical modeling of the controlled drug delivery formulations. A decade later, we have a new book entitled *Modified-Release Drug Delivery Technology* providing the latest comprehensive information on all controlled release formulations.

The book *Modified-Release Drug Delivery Technology*, edited by three leading scientists in the field, presents all currently available controlled release technologies and formulations. The book is divided into 10 different parts based on the delivery routes. The delivery routes described in the book are oral, colonic, ocular, oral mucosal, dermal/transdermal, injections/implants, nasal, vaginal, and pulmonary. The last part deals with the regulatory aspect of drug delivery technologies. There are a total of 80 chapters in the book written by experts who are at the forefront of each technology or formulation. Proper emphases were given to topics of current interests, such as colonic delivery in general, oral mucosal delivery including fast-dissolving tablets, transdermal delivery using microneedles or needle-free devices, and pulmonary delivery. The book covers all formulations and references available until 2000. The three editors did an incredible job in making all chapters coherent in the presentation style. Each chapter presents introduction of a technology, historical development, description of a technology, research and development, regulatory issues, and technology position and competitive advantages. Some chapters include future direction/outlook on the technologies described, and such information is useful in understanding the potential new applications as well as developing hybrid systems with other technologies. This is the book that every scientist in the controlled drug delivery area should have. This is one of an armful of books that the contents and quality of information justify the price of the book.

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Drug Delivery Systems in Cancer Therapy. Cancer Drug Discovery and Development. Dennis M. Brown, Ed. Humana Press, Totowa, NJ. www.humanapress.com. 2004. 390 pp. $165.00.

Cancer chemotherapy is one of the largest fields of drug delivery applications both in research and development. Drug delivery systems against cancers involve so many methodologies and technologies in their basic research, preclinical developments, and clinical practices due to a large diversity of cancers. It is almost impossible to clinically recognize cancers as a single disease. The methodology of drug targeting to solid tumors is totally different from that to leukemia. Even among solid tumors, significant differences are observed in key factors for successful drug targeting, such as flow, density, and permeability of tumor blood vessels, and sensitivity of tumor cells against anticancer drugs. Most books with "drug delivery (or targeting) of anticancer drugs" in their titles mainly focus on the concept, methodologies, and technologies of drug delivery (or targeting), but only a few books including this book provide concise and easily understandable clinical significance, current status, and future perspective of anticancer drug delivery.

This book is composed of four parts. Part 1 describes pharmacological consideration of anticancer drugs by explaining basic and clinically important subjects, such as routes of injections, theoretical and clinical significance of regional injection, and optimization of drug exposure to cancer cells. These are common subjects in the field of clinical oncology, but not frequently described in books in the drug delivery field. This part represents unique characteristics of this book and is important for researchers in the field of drug delivery systems, drug targeting, and pharmaceutical sciences. Part 2 presents a concise summary of drug carrier technologies and describes biopolymers, hydrogels, microparticles, emulsions, and poly(ethylene glycol) conjugation to proteins. Part 2 covers various drug carrier technologies, but lacks liposomes, water-soluble synthetic polymers, and polymeric micelles. Liposomes are described in Part 3 with a focus on clinical aspects. Part 3 introduces several drug delivery systems available in the current cancer chemotherapy including liposomal targeting and sustained release delivery of anticancer drugs by local injection, followed by brief summary and perspective of cancer vaccines. Part 4 is used for novel therapies of cancer, such as gene and antisense therapies.

This book is mainly written from the viewpoint of clinical practice in cancer chemotherapy and is full of clinically important information. This book is highly recommended for researchers who possess basic knowledge of drug targeting and/or delivery technologies and want to know clinical aspects of anticancer drug delivery. This book is also very informative for clinical oncologists who want to know the frontier of drug delivery.

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Drug Bioavailability. Estimation of Solubility, Permeability, Absorption and Bioavailability. H. van de Waterbeemd, H. Lennernäs, and P. Artursson, Eds. (Methods and Principles in Medicinal Chemistry, Volume 18). Wiley-VCH, Weinheim, Germany. www.wiley-vch.de. 2003. 579 pp. $195.00.

This book covers the different areas of research pertaining to drug delivery that must come together in a coherent and complementary way during the drug discovery and early development phases for new pharmaceutical products. Although some references are made to other routes of administration, this book focuses on the state-of-the-science regarding the critical parameters, screening methods, experimental

techniques, and predictive models for the discovery and early development of drugs intended for the oral route of administration.

A publication such as this one is timely for different reasons. One being strictly technical, the other, by no means less significant, comes from the current environment in the pharmaceutical industry. From a technical standpoint, the book covers in good detail the advancements in the study, screening, and prediction of the parameters that determine the fate and transport of drug molecules in the gastrointestinal (GI) tract. This is done from the perspective of the physicochemical properties of the molecule as well as from the interaction of the drug entity with the proteins expressed by living cells that influence drug transport. The book provides an extensive discussion of the role of transporters and metabolic isozymes, the combined roles they play in drug absorption, and the ways they are being incorporated into the design of *in vitro* screening methods. From a nontechnical point of view, this book has the potential to serve as a very useful common ground for discussion when it comes to information exchange between laboratories. The consolidation and globalization of the pharmaceutical industry continues to bring unanticipated partnerships. It is not uncommon that one-time separate laboratories (parts of semi-independent research centers of an organization or even parts of formerly competing corporations) are suddenly faced with the prospect of exchanging information and harmonizing their practices for the screening of solubility, permeability, and metabolic liabilities of their molecules. This book does a very good job in reviewing the most common variants in this type of screening and in illustrating why and in which way the corresponding results can be expected to vary.

The first of five sections in the book covers permeability and absorption. The chapters are arranged such that there is a logical flow that begins with a discussion on the role that the physicochemical attributes of the molecule have on drug absorption. Then, the different high throughput screening (HTS) methods are covered. The HTS methods discussed cover the span going from physicochemical parameters to permeability using both cell lines and artificial membranes. The book provides a very clear and extensive discussion about the specific experimental conditions used for measuring different physicochemical parameters, the different cell lines and their differences/similarities, as well as the different laboratory practices used in HTS today. The section on *in vitro* methodologies is followed by the *in vivo* assessment of permeability and absorption, covering the use of animals and studies with humans.

The second section of the book focuses on solubility and dissolution, with the emphasis heavily placed on dissolution. Solubility is covered more from a biopharmaceutical standpoint, namely, the impact of solubility as a driving parameter, rather than the molecular causes of a high or low solubility value. The book does include a chapter on statistical models for structure-property relationships on solubility, but this part is by no means extensive. This section includes a very interesting discussion on how the advent of HTS technology has altered the solubility test itself, specifically, in regard to the physical form of drug samples used for testing during discovery and to the type and reliability of the solubility values obtained.

The third section of the book covers the role of transporters and metabolic isozymes on oral absorption. This section provides a detailed discussion on drug transporters found in the GI tract and in the liver. The presence and levels of different transporters is discussed in relation to the anatomy of the GI tract. In addition, the interplay between drug transporters and metabolic isozymes, whose combined effect is what counts in the end, is covered also with the varying anatomy of the GI tract in mind. This section ends with a chapter on the use of genetically modified cell lines made to express different transporters and metabolizing enzymes for *in vitro* screening.

The next section in the book focuses on the use of computational methods for predicting drug absorption and bioavailability. Molecular descriptors for the geometry and interactive properties such as hydrogen bonding of drugs are covered. The role of molecular surface area, specifically polar surface area (PSA) and its relationship to drug absorption, is covered with particular detail. The computational value of PSA as a composite parameter that carries information that goes beyond molecular geometry is discussed in relation to the drug's absorption attributes. This section includes a practical review on absorption, distribution, metabolism, and elimination (ADME) modeling using available software, and the use of one of such packages to build on the well-known rule-of-five criterion for drug selection is also covered. This section also includes an interesting review on novel computational methods used to identify multiple substructural recognition patterns in a molecule for purposes of establishing structure-activity relationships for P-glycoprotein.

The last part of the book deals with aspects of drug development. This is a series of loosely connected chapters that deal more with the implications and the strategic aspects of drug selection. In this section, the current and potential future impact of the biopharmaceutical classification system (BCS) is discussed. Other aspects such as methodologies for finding, and feasibility of obtaining, *in vivo/in vitro* correlations are also discussed.

The book consists of a collection of individually authored chapters, each with a specific focus. A publication of this nature makes some degree of overlap unavoidable. For the most part, however, the book does a good job in keeping the overlap limited to that needed for healthy flow of the subjects covered, without duplication of the material included. The book can serve as a reference; each chapter can be individually consulted for its contents on a specific subject. At the beginning of every chapter, a list of the abbreviations used is provided, although the reader should be forewarned that not every abbreviation used in the book is included in such lists. Nevertheless, although not all encompassing, the lists of abbreviations at the beginning of every chapter are quite helpful. The notation used in the book corresponds to that of the published literature on each subject, with the specific variations preferred by the individual contributors to the book. This means that it is possible for P_{eff} and P_{eff} to represent different concepts in two sequential chapters (as it is actually the case in Chapters 7 and 8, for example). Fortunately, the use of similar notation types is not much of a problem, considering the different contexts in which they appear.

In general, this book would make a valuable resource for scientists working in drug discovery and early drug development, who are involved in the generation and/or technical evaluation of data pertaining to the absorption and ultimate bioavailability of drugs and drug candidates. Practitioners of

any of the different subspecialties covered in the book (e.g., physical property and solubility screening, permeability screening with cell lines or artificial membranes, *in vitro* metabolism screening, *in vivo* assessment of absorption and bioavailability and computer modeling) will find in this book an up-to-date review that includes enough detail to serve as a working reference, and one that also includes complete references in its bibliography. Because the book covers the different aspects related to drug absorption and bioavailability, it should also be a valuable resource for technical teams responsible for the drug selection process. Drug selection is predominantly, but not entirely, a technical question. There is an important strategic component to drug selection involving aspects such as business case, project management, and the clinical program. Nonpractitioners involved in the drug selection process would certainly benefit from access to the materials covered in this book.

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Clinical Skills for Pharmacists. A Patient-Focused Approach. Karen J. Tietze. Mosby, St. Louis, MO. www.elsevierhealth.com. 2004. 241 pp. $39.95.

This is a dense and informative book with many attractive features. Thus, its clear structure and interesting approach invite reading. Indepth study is encouraged by the didactic format of the chapters, which begin with learning objectives and end with self-evaluation questions. Study is also facilitated by the many relevant examples and practical cases provided and by a comprehensive and accurate subject index. The primary readers of the book will be clinical pharmacists and students in this discipline. However, a number of other health professionals are also expected to benefit greatly from this book. Thus, physicians and nurses may gain a better appreciation of the skills and competences they can expect from their pharmacist colleagues. Community pharmacists, not to mention pharmacy students, will find it an invaluable source of information and knowledge. It is even our feeling that other professionals associated with drug development (e.g., biologists and pharmacologists) and clinical trials (e.g., bioanalysts and statisticians) may like to keep this work as a useful reference, as it can offer a better understanding of the clinical context and objectives of their work.

The book contains 10 chapters that can be grouped in 4 parts: 2 introductory chapters; the physiopathological context of the clinical pharmacist's activity; specific medicinal and therapeutic skills expected from clinical pharmacists; and a concluding chapter on ethics whose validity extends to all health professionals. A short introductory chapter sets the scene by offering a cogent and inviting overview of patient-focused pharmacy practice, the clinical environment, the health care delivery system, and the roles and responsibilities of the various partners. In the second chapter, the author presents communication skills for the pharmacist in a clear and engaging manner. Body language, verbal and written communication, medical jargon as a source of confusion, integration with the interlocutor (various types of patients, physicians, and fellow pharmacists), the art of teaching and lecturing, are explained with text, tables, and figures. The theme of this chapter is quite original and unexpected, but the reader will not fail to recognize its significance and value. Indeed, what are prescriptions and recommendations worth, if they cannot be transmitted to the intended recipient for lack of communication skills?

The next four chapters present the physiopathological context in which the clinical pharmacist operates. Obtaining and compiling the medication history of patients is the first subject to be examined. Here, the emphasis is on the essential role of clinical pharmacists in acquiring and documenting medication histories, a major goal of which is to assess the patient's compliance as a key factor of therapeutic success. Like all other chapters, this one is well-structured, systematic, practical, and very informative. In the next chapter, the physical assessment techniques used by physicians are explained for each organ system in turn, with a focus on examination techniques and instruments; there is also a generous compilation of terminology and acronyms to help understanding medical parlance. Mastering this type of information is very clearly a *sine qua non* condition for clinical pharmacists to be able to communicate with physicians. The same is true of the laboratory and diagnostic tests reviewed in the next chapter together with many reference values. Again, the reader finds here a systematic, concise, informative, and dense text whose layout confirms the remarkable pedagogical talent of the author. All this medical information must then be structured into a patient case presentation that clinical pharmacists must be conversant with and to which they make essential contributions. This is the subject of Chapter 6, which weaves examples, flowsheets, diagrams, and a no-nonsense text into an outstanding lesson.

The third part of the book covers the specific medicinal and therapeutic skills of the clinical pharmacist. These include therapeutic planning (Chapter 7), monitoring of drug therapies (Chapter 8), and finally researching of drug information and providing the information to health professionals (Chapter 9). During their undergraduate and graduate studies, aspiring clinical pharmacists need to ingest huge amounts of information in the pharmaceutical and biomedical sciences and to assimilate it into knowledge. In the current book, they will learn how to put this information and knowledge to good use in the service of health care. They will be instructed how to identify and prioritize a patient's medical problems, how to develop a specific therapeutic plan, how to select specific therapeutic regimens, and how to design and conduct the monitoring process. Such instruction is not simply theoretical, however, as it is illustrated with the detailed analysis of complex and credible patient case examples.

The chapter on drug information is outstanding in insisting more on quality than quantity. Indeed, quality is the prime criterion given that the relevance and accuracy of treatment data depend to a large extent on the pivotal role of clinical pharmacists. Though the printed information sources listed here are very largely American, the lesson on how to critically evaluate such sources is universal. Not only are the readers urged to critically appraise any source, they are also taught how to do so comprehensively and systematically. In fact, the list of questions to ask when assessing Web sites, textbooks,

literature reviews, or primary research papers has universal value for each and every scientist.

The book concludes with a welcome chapter on "Ethics in pharmacy and health care." Again, the value and scope of this chapter go way beyond clinical pharmacists to all health care professionals. Of course nurses, physicians, and pharmacists have their own, specific codes of ethics that this chapter cogently presents. But their quintessence is the same, and it is the respect of and empathy with patients in particular, and our human fellows in general. In a time when justice is spoken of more often than it is practiced, we as health professionals have a strong duty to serve as examples. It is not the least merit of this little but great book to insist on this duty.

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Chronotherapeutics. Peter Redfern, Ed. Pharmaceutical Press, Grayslake, IL. www.pharmpress.com. 2003. 426 pp. $115.00.

When I was asked to review this book, I was quite intrigued because I was of the opinion that chronopharmacology studies have a sort of Ripley's Believe It Or Not flavor to them. Contrary to my beliefs, this book highlights the great deal of science that has been put toward explaining biological rhythms and how to exploit them for therapeutic benefit. The book has 15 chapters broadly divided into chronophysiology, chronopathology, chronopharmacology, and chronotherapeutics. The chapters on physiology go into detail on measuring rhythms (albeit there is little in the way of directing how to analyze or model such data), the biological clock, hormonal rhythms, and the effect of aging on melatonin secretion. These chapters were full of details on the mechanisms behind biological rhythms, such as the innervation and neuropathways of the suprachiasmatic nucleus and gene products of circadian oscillators. Particular attention was shown throughout the book on the importance of zeitgebers (external stimuli such as activity-inactivity, light-dark, food availability-unavailability) in synchronizing biological clocks and the role of melatonin. However, as no drug has been shown to selectively affect biological rhythms, outside of exogenous administration of melatonin itself, these chapters are more of theoretical interest and do not directly relate to the therapeutics chapters in the book.

The chapters on what I will broadly define as chronopharmacology begin by discussing how circadian rhythms affect the pharmacokinetics of many drugs. The authors present some plausible explanations for why altered hepatic blood flow at night might affect the clearance of highly extracted drugs if administered in the evening, and give many, many examples of drugs that have shown pharmacokinetic alterations when dosed at different times of the day but never really discuss why these drugs were studied in the first place. What made these researchers pick a particular drug and study it for its chronopharmacokinetics? Was it a serendipitous finding or did clinical evidence suggest a difference? What characteristics in a new chemical entity would suggest that a change in pharmacokinetics or pharmacodynamics would occur with dosing at different times of day? When should chronopharmacology be considered in the development a new drug? This information would be of interest to those of us in drug development. The chapter on pharmacodynamics was small, focusing on how receptor, enzyme, and ion channel activity may change during the day. I thought the authors had a tremendous opportunity to discuss how some of the best-selling drugs sold today, the statins for control of cholesterol, take advantage of the circadian rhythm of HMG-CoA reductase and request that patients take their medicine at night, corresponding to the peak time of cholesterol synthesis. This was only briefly mentioned. The chapter on chronopharmaceutics read like a compendium of oral time-delayed drug delivery systems that was quite heavy on actual physical descriptions of the products with little rationale for why one particular formulation might be more advantageous over another, outside of "Gee, look what we can do" factor.

The chapters on therapeutics covered a variety of topics, including asthma, cardiovascular disease, and cancer. This is where the book really shines. As no drug has been shown to modify the biological clock, outside of exogenous administration of melatonin, the therapeutic chapters focus on how time of day can alter efficacy and/or toxicity. For example, evening administration of nonsteroidal anti-inflammatory drugs (NSAIDs) to patients with osteoarthritis was shown to be more effective in patients with nocturnal or early morning pain, whereas administration in the morning or at noon was most effective in patients with peak pain occurring in the afternoon or evening. At the same time, other studies have shown that NSAID side effects are greater in the morning than in the evening. Hence, it is possible with some drugs to change the efficacy and side-effect profile simply by changing when the drug is given—a concept that, in my experience, is not given much thought in drug development.

The ability to modulate a drug's pharmacology simply by changing the time of day the drug is administered opens whole new areas of research for clinicians and drug developers. Overall, the book does a tremendous job in presenting an almost encyclopedic reference on chronotherapy and provides a nice comprehensive overview of the area.

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Hydrolysis in Drug and Prodrug Metabolism. Chemistry, Biochemistry, and Enzymology. Bernard Testa and Joachim M. Mayer. Wiley-VCH, Weinheim, Germany. www.wiley-vch.de. 2003. 780 pp. $215.00.

One of the most appealing aspects of this book is the consistent flow of writing style and format. This is undoubtedly because the book was written mainly by one person, Professor Testa, with untimely death of Dr. Mayer. Generous space was given to superbly and accurately drawn figures and

well-placed tables for quick summary. The sense of continuity together with tight organization of massive amount of information that has never been compiled in any one place truly makes this book an invaluable desk reference. This is particularly true for chemists embarking on prodrug design.

The introductory chapter, which is primarily concerned with definitions, is followed by classification, localization, and some physiological roles of peptidases and esterases in Chapter 2 and the catalytic mechanisms of hydrolytic enzymes in Chapter 3. The content of these two chapters sets a stage for detailed discussions throughout the book. Together it should provide chemists with a knowledge basis for incorporating substrate specificity as well as intracellular activation (if desired) in prodrug design. Chapters 4 through 6 are devoted to amide hydrolysis: acyclic amides including imides, lactams, and peptides, respectively. Each chapter has an extensive list of examples peppered with discussion on structure-metabolism relations. Chapter 5 is exclusively for lactams, mainly and justifiably for beta-lactam antibiotics. Of these three chapters, discussion on peptide hydrolysis (Chapter 6) received most space, 130 pages. This chapter includes an extensive treatment of nonenzymatic, but intramolecularly catalyzed, hydrolysis as well as pseudopeptides and peptidomimetics.

As in the case of amides, three chapters are devoted to the discussion on ester hydrolysis: Chapter 7 deals with basic hydrolysis mechanism involving carboxylates, including lactones and thioesters, whereas the other two chapters are for ester prodrugs and inorganic acid esters. Prodrugs containing an ester function are most commonly found for parent compounds with either a carboxylic acid or a phenol or alcohol, and indeed a long chapter of 115 pages is dedicated to the subject (Chapter 8). The cleavage of esters of inorganic acids is covered in Chapter 9. This includes the de-esterificationn of organic nitrates and nitrites and the cleavage of a large variety of organophosphates such as medicinal phosphate esters, industrial phosphate triesters, and the infamous P-halide compounds. The shorter Chapter 9 brings a clear classification of these and many structurally diverse xenobiotics and is just right for the subject. The final two chapters of the book deal with epoxide hydrolysis, a highly important class of metabolites of considerable toxicological significance, and some rather rare reactions such as covalent hydration and dehydration, not to mention the hydration of antitumor platinum compounds and its therapeutic significance. All in all, the major chapters are: Chapters 2 and 3 for overview, Chapters 4 through 6 for amide prodrugs, and Chapters 7 through 9 for ester prodrugs.

A cursory spot check yields the following comments. Information flow between chapters is facilitated by extensive cross-referencing, but it could have been made even better: for example, β-lactamase discussed on p. 24 can be connected to ADEPT described in Chapter 6. Discussion on aspartic hydrolases on p. 60 could be similarly coupled to pseudopeptidyl HIV-1 protease inhibitors discussed in Chapter 6 on p. 347. Missing from Chapter 3.6 is matrix metalloproteinases (MMP), a potentially hot subject in site-specific activation of anticancer prodrugs. Macromolecular prodrugs, which received only a brief treatment of one page, deserve an extended discussion in that many biotechnology-derived therapeutic agents are macromolecules (e.g., proteins and nucleic acids) and many macromolecules such as antibodies and albumin can serve as a pro-moiety. Particularly a pharmacokinetic analysis of macromolecular prodrugs could have been rather timely and fashionable. Intramolecular catalysis discussed at various places can be further exploited in designing sequentially labile prodrugs. Admittedly, this book is restricted to the chemistry, biochemistry, and enzymology of hydrolytic reactions, hence, addition of these subjects could be beyond its the scope. However, such comments address specific points and should not hide the appeal and scientific value of this work.

For the first time, the metabolic reactions of hydrolysis (enzymatic and nonenzymatic) of drugs, prodrugs, and many other xenobiotics are tightly and comprehensively organized under a single cover. The book clarifies and classifies the innumerable types of functional groups and substrates undergoing metabolic hydrolysis or hydration and gives due consideration to the therapeutic or toxicological implications of the reactions under discussion. As such, its didactic and formative value goes well beyond that of a simple collection. Having studied the book and surveyed its extensive table of content, the reader will not fail to be impressed by the huge (and not always fully recognized) metabolic realm existing between the redox reactions catalyzed by various oxidoreductases, such as the cytochromes P450, and the conjugation reactions catalyzed by many transferases.

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Protein Misfolding and Disease. Principles and Protocols. Peter Bross and Niels Gregersen, Eds. (Methods in Molecular Biology, Volume 232). Humana Press, Totowa, NJ. www.humanapress.com. 2003. 318 pp. $99.50.

This book introduces the concept of protein misfolding and its associated defects that are commonly referred to as conformational diseases. The book consists of three sections: General Concepts and Models; General Methods; and Techniques in Conformational Disease Research. Although there is some redundancy between the different sections, the individual chapters encompass valuable information for researchers in this burgeoning scientific area. The first section classifies conformational diseases according to their pathogenesis. Specific examples include cystic fibrosis, α-1 antitrypsin deficiency, Parkinson's disease, and aberrant protein folding as a molecular basis of cancer. This section also introduces yeast as a model system for studying protein folding mechanism.

In the General Methods section, a succinct introduction on recombinant protein is presented, followed by a compilation of available expression systems as experimental tools. The chapter on basic techniques of protein expression, site-directed mutagenesis, and pulse chase protocols provides useful case-study protocols. The third section consists of individual chapters dedicated to techniques for studying protein misfolding in diseases. These chapters provide great experimental detail and are an asset to any lab working on similar

systems. The book provides the researchers cook-book protocols that are simple in nature and may be useful also to researchers interested in the folding of recombinant proteins that do not play a role in conformational disease.

An area that is overlooked in the current book is that protein folding and misfolding can be studied readily using straightforward biophysical techniques, and a separate section on these techniques would have completed this volume. Overall, this is a very sound book that provides a solid background in conformational disease and presents the reader with helpful experimental protocols for studying protein folding and misfolding.

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Gene Transfer and Expression of Mammalian Cells. Savvas C. Makrides, Ed. Elsevier, Amsterdam. www.elsevier.nl. 2003. 680 pp. $220.00.

This book consists of a compilation of chapters that answer questions related to protein production in mammalian cells. The choice of using mammalian cells for the production of proteins should be based on an indepth analysis of the biotechnological needs to be met. Mammalian cells have a number of advantages over other host systems. They can fold complex proteins properly and they can produce both N-linked and O-linked glycosylation patterns. Moreover, their post-translational modification capabilities (e.g., maturing of proteins by proteolytic processing) are often superior to other host cells. These advantages come with some drawbacks. Mammalian cell culturing is expensive because of the use of rather expensive media, and downstream processing is rather complicated because of the potential risk of the presence of viruses, prions and mycoplasma.

This book lists 25 chapters and has a total of 659 pages of text. A major fraction of the book is taken up by describing the different virus-based vectors for gene expression: herpes simplex virus, Epstein-Barr virus, SV40 (simian virus), adeno-associated virus, adenovirus, vaccinia virus, baculovirus, coronavirus, poliovirus, Sindbis virus, Semliki Forest virus, retrovirus, and lentivirus. Attempts were made to structure all these contributions so that they give both basic and practical information. Two rather short chapters are devoted to discussion of nonviral transfection systems.

A subsequent chapter deals with reporter genes and discusses green fluorescent protein, luciferase, alkaline phosphatase, chloramphenicol acetyltransferase, and beta-galactosidase. Then, a number of chapters describe current ideas on the selection of proper plasmid/DNA backbones. Protein folding, protein glycosylation, and metabolism (e.g., proteolysis and RNA degradation) are extensively handled in a series of chapters. The last chapters are devoted to inducible gene expression systems and large-scale production of proteins in mammalian cells *in vitro* and in transgenic animals plus a short description on protein purification protocols.

The chapters are well organized and written by experts. The art work is expertly done. This book offers a wealth of valuable information to those who have to identify the preferred production protocol for their particular recombinant protein in mammalian cells.

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Gene Delivery to Mammalian Cells. Volume 1: Nonviral Gene Transfer Techniques. William C. Heiser, Ed. (Methods in Molecular Biology, Volume 245). Humana Press, Totowa, NJ. www.humanapress.com. 2003. 301 pp. $99.50.

Gene Delivery to Mammalian Cells. Volume 2: Viral Gene Transfer Techniques. William C. Heiser, Ed. (Methods in Molecular Biology, Volume 246). Humana Press, Totowa, NJ. www.humanapress.com. 2003. 565 pp. $125.00.

Volume 1 on nonviral gene transfer techniques is a collection of multi-authored chapters, mainly consisting of gene delivery using chemical and physical methods. All chapters contain a unique format consisting of introduction, materials, methods, and notes (conclusions). Each chapter presents its contents in a descriptive manner so that the readers will find the information easy to understand. Part I includes various carriers, such as DEAE-dextran, peptides, dendrimer, polyethyleneimine and cationic liposomes. Design methods and characterizations of the carriers are described in detail, and thus those who want to compare different methods would find the information highly useful. The currently available physical delivery methods discussed in detail are microinjection, particle bombardment, electroporation and hydrodynamic delivery. Volume 1 is highly beneficial to the gene delivery researchers, especially to the beginners who are looking for basic knowledge, current status and experimental protocols. Volume 1, however, lacks several important concepts and areas, such as targeted site-specific delivery and novel biodegradable and/or pH sensitive polymers, to name a few. There are no chapters that focus on the mechanisms of DNA delivery aiming to endosomal disruption, fate in lysosome, and nuclear localization, and so forth. This volume could have been strengthened if it included the administration routes with systemic, site-specific, and local gene delivery. In addition, the volume could have included chapters on experiments with different cell lines in *in vitro* and *in vivo* animal models for the specific diseases, such as cardiovascular defect, diabetes, cancer, and inflammatory disease.

Volume 2 focuses on basic knowledge and application protocols of viral gene transfer techniques. It covers most of the current viral gene transfer techniques using adenoviruses, adeno-associated viruses, herpes simplex viruses, baculoviruses, lentiviruses, retroviruses, and alphaviruses. Part I presents the delivery using adenoviruses. The first chapter

describes the biological background and application of the viruses. In addition, the limitation and improvement strategy of adenovirus for gene delivery are explained well. The next chapters present the protocols for gene delivery to muscle, liver, ling, spinal cord, and so forth. These chapters also include brief explanation on the current research status of the vector to specific organs. The proposed protocols will be useful for the researchers who are planning gene delivery to those organs. Part II presents gene delivery techniques using adeno-associated viruses. This part starts with an introductory chapter that shows background of the viruses, followed by specific topics of gene delivery to liver, lung, heart, brain, tumor, and hematopoietic stem cells. The other parts describe gene delivery using herpes simplex viruses, baculoviruses, lentiviruses, retroviruses, and alphaviruses in the same format as in the previous parts. Each part begins with a brief biological background and provides brief but effective understanding of each virus. The introductory chapter is followed by practical approaches using the viral vectors. The chapters are composed of introduction, required materials, step-by-step methods, and notes, providing important and practical comments for experimental procedures. This volume will be very useful to those who have just started gene transfer research, as it presents basic knowledge, current viral gene delivery strategies, and protocols. The topics that could have been included for advanced readers are targeting of viruses to specific organs or tissues, specific expression using tissue-specific promoters or enhancers, administration route specific to specific disease models, and modification of viruses using polymer such as PEG. The absence of those topics, however, does not diminish the high enthusiasm on this volume. It still presents more than enough up-to-date information on viral gene transfer techniques. Overall, this two-volume set serves as a valuable source of information on nonviral and viral gene delivery.

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Stem Cells Handbook. Stewart Sell, Ed. Humana Press, Totowa, NJ. www.humanapress.com. 2004. 509 pp. $175.00.

At the end of the 1950s, Till and McCulloch discovered that lethally irradiated mice with the ruined blood producing system could be saved by simple injection of bone marrow–derived cells taken from healthy mice. The survival of the transplanted mice was due to the restoration of the system by the transplanted bone marrow. Successive animal studies showed that the early phases of recovery were accompanied by the appearance of distinct colonies of donor cells in the spleens of the recipient mice. Each colony was the result of the capture and subsequent proliferation of a special type of donor cells, so called a stem cell. Current clinical practice of bone marrow transplantation, such as for the treatment of leukemia, is a direct consequence of this pioneering mouse investigation and attests to the extraordinary plasticity properties of stem cells. Also, in 1992 Reynolds and Weiss isolated cells from mouse brain and demonstrated that these cells could be cultured and multiplied as cellular aggregates called neurospheres. By controlling of the growth condition, these cells could be induced to differentiate into two different brain cell types, neurons and oligodendrocytes. In 2000, Clark *et al.* demonstrated that neurospheres could be differentiated into many unrelated cell types, such as kidney, liver, bone, and so forth. These dramatic discoveries have now been extended to a wide variety of enriched adult as well as embryonic stem populations prepared from diverse tissue sources. For instance, heamatopoietic stem cells can differentiate into liver and muscle; neural stem cells can form skin, lung, blood, muscle, kidney, and other cell types; muscle-derived stem cells can rearrange chondrocyte and all types of cells; mesenchymal stem cells normally responsible for bone and cartilage can differentiate neurons including other brain cell. Very recently, in 2004 Hwang *et al*. showed that it is possible to apply a pluripotent human embryonic stem cell line derived from a cloned blastocyst using somatic cell nuclear transfer techniques in tissue repair and transplantation medicine.

Rapid development and expansion of the adult and embryonic stem cells as pluripotent progenitors for various tissues have led to an even greater appreciation of the power of stem cells during the past several years. In terms of vast possibilities for treatment of congenital deficiency diseases as well as for regeneration of damaged tissues, this handbook provides in one source both the background and the current understanding of what stem cells are and what they can do. This handbook is composed of 43 chapters with 77 contributors who were selected for their significant contributions to and expertise in various aspects of stem cell biology. The first part of the book includes the function of embryonic stem cells in early development and organogenesis (Chapters 1–4), germinal stem cells in reproduction (Chapter 5), and cloning and programming of embryonic stem cells (Chapters 6 and 7). The crucial role of stem cells in amphibian regeneration and mammalian wound healing shows the potential of these cells for true tissue resprouting in Chapters 8 and 9. These chapters present the fundamental concepts on the types of cells from origin, mammalian differentiation and development in term of the stem cell level, gene therapy for stem cells, therapeutic cloning and genomic imprinting in embryonic stem cells, and signaling and regulation of stem cells.

The second part includes applications of stem cells in tissue regeneration for various organ systems, such as musculoskeletal tissue (Chapter 10), blood (Chapters 11–15), nervous tissue (Chapters 16 and 17), retina (Chapter 18), blood vessel (Chapter 19), heart (Chapters 20–23), kidney (Chapters 24 and 25), skin (Chapters 26), glandular organs (Chapter 28), gastrointestinal tract (Chapters 29 and 30), liver (Chapters 31–36), pancreas (Chapters 37 and 38), mammary gland (Chapter 39), prostate (Chapter 40), and lung (Chapter 41). Each chapter describes experimental methods such as isolation and characterization of various stem cell types, potential for their manipulations, and possibilities for future therapeutic applications in experimental models and in human diseases. The chapters show the possibility that almost all organs in the body can be made from any stem cell sources by controlling the cell culture environment. That is to say, neurons can be formed from any type of progenitor cells, such as bone marrow-derived stem cells, hematopoietic stem cells, muscle-

derived stem cells, fat-derived stem cells, and so on. The last chapter (Chapter 43) by Doyonnas and Blau introduces the future of stem cell research with 24 fundamental questions.

This handbook is well-organized to provide comprehensive information and many examples for clinical applications. Several chapters deal with the remarkable properties of hematopoietic stem cells and the clinical results achieved by transplantation of bone marrow stem cells. The book emphasizes the potential future potential in clinical applications for regeneration of muscoskeletal, cardiovascular, and nervous system as described in preclinical models. Cell therapy and gene therapy are described for each organ. This handbook might be aimed at researchers, graduate students, and mature scientists with a basic knowledge of regenerative medicine. Even though the field of stem cells is changing fast, the abundant references in the book will be very useful to beginners and undergraduate students for studying the history and designing the experiments. This handbook provides huge amounts of methodological information on identification, characterization, and assay, such as histology, immunohistochemistry, tracing, and confirmation of stem differentiation and transdifferenciation into other tissue cell types. In summary, this book is a highly useful, concise encyclopedia providing introduction to stem cells as well as special topics in the state-of-the-art stem cell research.

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Cell Cycle Checkpoint Control Protocols. Howard B. Lieberman, Ed. (Methods in Molecular Biology, Volume 241). Humana Press, Totowa, NJ. www.humanapress.com. 2003. 372 pp. $99.50.

It is clear that understanding events involved in the cell cycle is of central importance to providing methods of regulating this crucial event to control the growth and fate of cells. As one might imagine, the applications of research on this basic cell function are many-fold and extremely diverse. One can envision this data can provide lead candidates to fight cancer as well as stimulating the replication of yeast to improve the production of beer—two areas I am particularly concerned with. The protocols related to cell cycle checkpoint control compiled by Howard Lieberman provide an extremely practical series of articles that describe how such studies have been performed in a number of leading laboratories. If I worked more directly in this field I am sure this text would have been quite useful for a number of the chapters. However, I do not work directly in this field and this is where I have trouble with the text.

I have read, purchased, reviewed and discussed with colleagues a number of books that focused on describing protocols in a defined or selected field of science. These have not always been in my area(s) of interest, but a number have captured my attention and garnered my respect because of how they were presented. A common thread of these texts has been their ability to present the subject in a manner that grabbed the reader by initially demonstrating the importance of the topic and then providing a framework of thought as to how the reader, regardless of their background or particular interest, would benefit from some aspect of the protocols presented. Unfortunately, I did not get any of this from this text—and really I tried looking for it. Several of the chapters have a reasonable introduction but in general most chapters and the book itself misses on these points. This does not preclude the usefulness of this collection of protocols for those embroiled in the field and for whom no introduction is needed. What it does do, however, is to limit its interest and accessibility for those of us outside or on the periphery of this field.

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Vaccine Protocols. Second Edn. Andrew Robinson, Michael J. Hudson, and Martin P. Cranage, Eds. Humana Press, Totowa, NJ. www.humanapress.com. 2003. 414 pp. $135.00.

This second edition in the *Methods in Molecular Medicine* series is intended for both novices and experts in the vaccine field. The aim of the book is to provide contemporary protocols and methods that will aid those interested in vaccinology. The book is composed of 24 chapters with the average chapter being 15–20 pages. In short, the book successfully serves its aim and may provide the reader with a ready off-the-shelf source of information and protocols that are otherwise not easily located. The editors have structured the book into three main sections. Section 1 (Chapters 1–10) describes the development and production of vaccines including viral, bacterial, subunit protein, and plasmid DNA-based vaccines. Section 2 (Chapters 11–20) describes techniques and methods to formulate vaccines and vaccine delivery systems as well as protocols to assess immune responses. Finally, Section 3 (Chapters 21–24) describes considerations and methods and protocols in the scale-up, manufacture, stability, quality assurance, and human clinical trials of vaccines.

Chapter 1 provides an excellent overview of vaccines, which in turn serves as a nice primer for the subsequent chapters (Chapters 2–10) on live viral vectors, attenuated salmonella strains, synthetic peptides, antigen delivery with bacteria, detoxification of bacterial toxins, and the preparation of polysaccharide-conjugate vaccines. Several of these chapters are very well written, but are quite specific in their subject matter. Chapters 11–14 pertain to pharmaceutical formulation of vaccines including adjuvant formulations, plasmid DNA vaccines, microencapsulation, and lyophilization. Chapter 12 on the incorporation of immunomodulators into plasmid DNA vaccines seems out of place in this section. Although the chapter is very well written and informative, it pertains to the use of interleukin-12 genes inserted in plasmid DNA vaccines to enhance or modulate the resulting immune

responses. Instead, a very nice overview on DNA vaccination strategies including formulation and delivery strategies is found later in Chapter 23. Chapters 15–20 provide various protocols in assessing mucosal immunity, cellular and T-cell responses, antibody responses, and animal models. These chapters also provide important information for those needing key protocols to assess humoral and cellular immune responses in animals. They are very clearly and effectively written and lay out specific protocols in a step-by-step manner. In particular, the three chapters on the detection of T-cell and antibody responses in animals are excellent and highly detailed. In my opinion, these are key chapters for novices (i.e., students, drug delivery experts, molecular biologists, and so forth) that are moving into the vaccine field and would greatly benefit from this information. Finally, Section 3 (Chapters 21–24) pertains to the scale-up, manufacture, stability, quality assurance, and clinical trial investigation of vaccines. These later chapters are especially suited for students but are likely too general for those with more experience in vaccine development.

The book has a number of strengths. The editors have assembled very well known and highly regarded scientists to contribute to the book. Except for the placement of a few chapters, the layout of the book is convenient and well thought out. Finally, most of the chapters provide protocols that readers will find very useful, as well as a comprehensive list of references. The book does have some weaknesses. For examples, a few chapters are very short and/or do not provide protocols or methods. One other weakness is that a few of the chapters address subject matter that is highly focused and thus may be of interest to a smaller number of readers. Overall, I concluded that the book is an excellent resource. More comprehensive reviews on the individual subject matter covered in the chapters can be found in the literature. However, a ready source of reviews accompanied by easy to follow step-by-step protocols cannot.

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Antibody Engineering. Methods and Protocols. Benny K. C. Lo, Ed. Humana Press, Totowa, NJ. www.humanapress.com. 2003. 561 pp. $125.00.

It is hard to imagine a class of proteins that have made a greater impact in more areas of science and medicine in the last 50 years than antibodies. In the body, antibodies represent a group of proteins that constitute a major component of our blood and the fluids that are expressed at the surfaces of our mucosal surfaces (such as the linings of the gut, lungs, and reproductive tracts). An antibody or immunoglobulin (Ig) produced by the body has a generalized structure where two heavy chain components associate to form a Y-shaped structure, to which two light chains interact with the arms of the Y. It is the alignment of terminal regions of light and heavy chains that constitute a unique binding site that allows antibodies to recognize structures with exquisite refinement—in some cases sensing the presence or absence of a single atom. The various classes of antibodies differ in several important ways, with the most basic being due to variations in amino acid sequences of their heavy chain domains. These differences provide the basis of antibody self-association. For example heavy chains of the A class of immunoglobulins (IgA) interact through their heavy chains to form a dimer of the basic antibody structure whereas molecules of the IgM class of antibodies form higher-order oligomers. It is also these heavy domain regions that provide the basis for recognition by a variety of cells of the immune system to allow for cell-mediated uptake and destruction of structures decorated by antibodies. This remarkable system of production and selective function make antibodies one the most crucial tools used by the body in its defense against pathogenic agents.

The advent of clonal selection of immortalized cells capable of making a single form of an antibody has been a tremendous advance to the use of (monoclonal) antibodies. Even greater impact, however, may have been derived from studies that provided an understanding of the structure and function of specific domains and components of antibodies. This information has allowed for the design of new antibodies and, greater yet, new antibody-like molecules—protein chimeras that contain complete antibodies or fragments of antibodies combined with other structures that can now be selectively targeted. Alternately, regions of the antibody molecule can be removed or modified to alter its function or properties; producing an antibody-like protein for a desired application. This capacity to generate these chimeras has lead to a number of novel therapeutics as well as incredibly useful laboratory reagents. All of these advances can be loosely captured by the term "Antibody Engineering," but I am not certain such a simple term truly captures the vast array of potential modifications that can be made starting from the basic framework of an antibody—particularly when one considers that this must include the design of an antibody structure based on desired functional properties and that the designed protein must be made in large quantities and at exceptional levels of purity.

Benny Lo has recently edited the book entitled *Antibody Engineering, Methods and Protocols* that covers all of this and more. I was extremely impressed by the layout of this text and found it to be very accessible for both the novice and the seasoned researcher in this field. Most texts that focus on pulling together methods and protocols focus on this task to the point of missing the bigger picture of putting the information in context and guiding the reader through a logical sequence that provides not only crucial, practical information but also the philosophy behind those methods that allows for a greater rate of success when applying this information. This text starts out with a set of Web sites for assessing structure and function relationships of antibodies (an excellent idea) and then builds on this with a series of excellent chapters on understanding and modeling antibody structures. The text then presents a series of chapters on physiological aspects of antibody design followed by methods to actually generate these antibodies at sufficient scale for their testing. Finally, the book closes with a series of contributions describing how to examine the function of these antibody-based materials and novel application using them that include catalytic antibodies and cancer treatments.

I found this text an absolute pleasure from start to finish.

It is a well-organized series of excellent entries from individuals doing superb work in their respective fields. This is the kind of book that I would recommend to a beginning student and to someone who has worked in the field for years. Clearly, such a text will find its way onto the office bookshelf of many scientists working on making therapeutic antibody applications a reality.

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