



## Book reviews

**A. Rolland, S.M. Sullivan (Eds.), *Pharmaceutical Gene Delivery Systems*, Marcel Decker, New York, 2004, 424 pp.**

Recent progress in human genome exploration and proteomics has offered unprecedented opportunities in turning genes into gene medicines. While viral vectors are known to provide high transfection, they have limited tropism and often cause immunostimulation. Nonviral vectors, on the other hand, show poor transfection but are relatively safe. Hybrid systems that combine the characteristics of both viral and nonviral vectors have the potential to provide efficient transfection, without inducing immune response. The publication of *Pharmaceutical Gene Delivery Systems* is timely. This is a unique book, which discusses the recent development of both viral and nonviral vectors in 15 different chapters. The 1st chapter provides an overview of gene therapy, product development process, regulatory issues and clinical trials.

Sustained gene expression is required for the treatment of several genetic disorders including cystic fibrosis, hemophilia, muscular dystrophy and lysosomal storage disorders. Chapter 2 discusses the following three basic requirements to achieve sustained production of therapeutic proteins at the disease targets: (i) stable transduction of the target tissue, (ii) maintenance of gene expression, and (iii) minimizing the immune response to the vector and transgene product. Regulated gene expression is important, since most therapeutic proteins are associated with side effects and toxicities when overproduced. Chapter 3 summarizes three categories of drug-dependent gene regulation systems, such as bacterial protein repressor/inducible system, dimerizer-inducible system and antiprogesterin-inducible system.

Despite their relatively poor transfection efficiency compared to viral vectors, cationic lipids maintain

their popularity among gene delivery scientists. Chapter 4 provides some insights on the development of cationic lipid formulations and discusses the factors influencing cationic lipid-based gene transfer, including stability in physiological medium, role of charge and particle size on cellular uptake, endosomal escape and nuclear entry. Importance of a quaternary amine headgroup, a fusogenic moiety and characteristic binding to cell surface heparin sulfate proteoglycans are also highlighted. Chapter 5 discusses how the conjugation of poly(ethylene glycol) and targeting ligands to cationic polymers can overcome different biological barriers to achieve target-specific gene delivery.

Problems associated with existing viral and nonviral vectors are discussed in Chapter 6. Efficient gene transfer without significant safety concerns can be achieved by using hybrid vectors utilizing components from both viral and nonviral vectors. Hemagglutinin Virus of Japan (HVJ) or other viral components can be used along with liposomes for enhanced gene transfer. Moreover, incorporation of Epstein Barr Virus (EBV) replicon in the plasmid vector can prolong the duration of transgene expression. Chapter 7 discusses various aspects of first generation, second-generation and fully deleted (gutted) adenoviral vectors. Chapter 8 discusses what improvements are needed in adeno-associated viral (AAV) vectors to provide persistent gene expression. Cellular uptake, intracellular trafficking, mechanism of genome persistence and host immune responses of AAV vectors are also discussed. Chapter 9 discusses how the retrovirus envelope modification can decrease the host immune response, especially by site-specific integration of retroviral vectors.

Chapter 10 discusses the use of gene gun, electroporation and sonoporation for gene delivery. In cancer gene therapy, an increasing number of preclinical and

clinical trials are employing nonviral vectors. Chapter 11 presents three gene therapy approaches to eradicate cancer cells, which include targeting specific genetic defects that endow cancer cells with growth advantage, immunocancer gene therapy and sensitization of cancer cells to drug treatment. Combination of different approaches may have better clinical outcome. Since replication-deficient adenoviral vectors have disadvantages in high-level expression of proteins in the tumor tissue, replicating vectors have attracted a renewed interest. Chapter 12 discusses about the use of replicating adenoviral vectors for cancer therapy and how to prevent deleterious effects of these replicating vectors. Strategies to confer selectivity to replicating adenoviruses are discussed including deletion of E1B-55K, deletion of the complete E1B region, partial or complete deletion of E1A, and expression of the E1A gene controlled by tumor-specific promoters. In addition, capsid modification for tumor targeting and codelivery of two complementary vectors are presented. Chapter 13 discusses cardiovascular gene therapy after local intravascular, perivascular and systemic administration. This chapter also summarizes the clinical applications of gene therapy for angiogenesis, restenosis, atherosclerosis/hyperlipidemia and stents. Chapter 14 highlights the recent progress in gene therapy of pulmonary disorders, with particular emphasis on cystic fibrosis,  $\alpha$ -1-antitrypsin deficiency and lung cancer.

Artificial chromosomes are DNA moieties created *in vitro* that behave like natural chromosomes *in vivo*. Chapter 15 discusses about the types and components of artificial chromosomes. Technology for the production of mammalian artificial chromosomes (MACs) has been outlined, and elaborated with highlight on the episomal MAC, which utilizes a component from the Epstein Barr Virus. This chapter discusses several possible applications of artificial chromosomes and the technical hurdles that have currently limited their development and use.

This book is well written and carefully edited. The editors have assembled a panel of international experts knowledgeable about the intricacies of gene medicines. The collection of chapters represents a comprehensive treatise on recent advances and current approaches that attempt to circumvent the problems associated with viral and nonviral gene delivery. I recommend this book to investigators working in this

field, and to all who wish to enhance their understanding of gene delivery and expression systems.

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**R.H.Guy, J.Hadgraft (Eds.), *Transdermal Drug Delivery, 2nd Edition, revised and expanded*, Marcel Dekker, New York, 2003, 383 pp.**

This book is Vol. 123 in the well-known Marcel Dekker "Drugs and the Pharmaceutical Sciences" textbook and monograph series, executive editor James Swarbrick. The first edition of this book was published in the late 1980's, and this new 2003 edition contains a concise summary of the predictive physicochemical property models for stratum corneum drug transport optimized during the last 15 years, as well as new physical approaches for drug transport enhancement in the skin.

The book contains eleven chapters, with the initial four dedicated to basic transdermal/topical drug delivery concepts and skin absorption prediction, and six dedicated to novel methods of transdermal/topical absorption improvement. After Chapter 1, an excellent introductory compilation by the editors, Chapter 2 provides a comprehensive skin permeability modeling review by Vecchia and Bunge. Chapter 2 has an exceptional comparative table summarizing all previously published skin permeability coefficient models, which contains models of data collected as early as Scheuplein's 1967 U.S. Army research. Another notable table in this chapter contains the Flynn database with 97 permeability measurements for 94 different chemicals, along with the fraction of nonionized chemical in the vehicle and the temperature of the diffusion experiment. Chapter 3 is a continuation of the Vecchia and Bunge analysis of skin permeability prediction from available databases. They examined 170 permeability coefficient measurements for 127 chemicals, ranging in molecular weights from 18 to