

ies, and translational studies in animal models are original work of the chapter authors. Presented in the broader context of transplantation biology, the importance of the experiments is highlighted and points strongly toward the potential for targeting chemokines and their receptors for therapies.

As stated by the series editor, Dr Lenfant, in his introduction, the volume as a whole, "takes the reader to the forefront of the field of chemokines... and opens the door on new research questions and ideas." Accordingly, the reader will probably have an appreciation of chemokines as natural targets for interventions in lung disease.

In summary, **Chemokines in the Lung** continues the excellence in the Lung Biology in Health and Disease series. It will serve as a valuable introduction to chemokines as well as an authoritative reference to the role of chemokines in lung disease.

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Gene Therapy in Lung Disease. Steven M Albelda, editor. (Lung Biology in Health and Disease series, Volume 169, Claude Lenfant, executive editor). New York: Marcel Dekker. 2002. Hard cover, illustrated, 555 pages, \$185.

The National Heart, Lung and Blood Institute at the National Institutes of Health publishes a series entitled Lung Biology in Health and Disease, under the guidance of the institute's director, Dr Claude Lenfant. For each volume Dr Lenfant selects a specific topic and an editor, who solicits contributions from leaders in the field and combines the contributions to make the final product. The goal is to produce a focused review on the most recent research, a thorough and balanced discussion of newer concepts and controversies, and future directions for research. Thus, these monographs are primarily intended for basic scientists and clinical researchers, as updates on the state of research in their field, and for researchers in training as reference tools.

Volume 169 in this series, **Gene Therapy in Lung Disease**, is edited by Steven Albelda. The book begins with an excellent historical overview that gives some fasci-

nating details on early events in gene therapy and important information on public policies about gene therapy clinical trials with humans. However, there is disappointingly little discussion on the events that led up to what many would consider the biggest setback to date—the death of a 19-year-old man in a trial of gene transfer of an adenoviral vector delivered into the liver, intended as therapy for ornithine transcarbamylase deficiency. That death put all human gene therapy trials on hold in the United States and precipitated intense public and government scrutiny of how these trials are conducted. Wivel, the author of the chapter on that subject, describes the important regulatory changes that followed the man's death, but given Wivel's experience in the field, I wished for some discussion on why that tragic event occurred and on what more we scientists can do to protect our research subjects from harm.

The next 4 chapters give extensive details on the major vector systems under development for gene therapy of the lung. The quality of these 4 chapters differs tremendously. For example, Duan, Yue, and Engelhardt's chapter on adeno-associated virus vectors is outstanding: there is an incredible amount of detail and elegant discussion on the problems and limitations of adeno-associated virus vectors, and possible solutions. The chapter gives a balanced view of the advantages and disadvantages of that vector.

In contrast, the chapter on cationic liposome/plasmid deoxyribonucleic complexes as a gene delivery vehicle is far from balanced. For example, much of the data on the liposome component of the complex is devoted to studies that used GL67, a lipid developed by the pharmaceutical company Genzyme. Another example of lack of balance is that the author used as evidence for efficacy of aerosol plasmid/liposome complexes a publication that deals primarily with the pro-inflammatory effect of the Genzyme GL67 lipid in humans. In that study 4 of the 8 cystic fibrosis patients who received an aerosol of a cystic fibrosis transmembrane conductance regulator-encoding plasmid complexed with GL-67 had a "pronounced clinical syndrome of fever (maximum of 39.6°C), myalgia, and arthralgia" (reference 57, Chapter 4). However, Scheule references this publication as a human study that "demonstrated that vector-specific transgene expression" had occurred and therefore sup-

ports the claim of potential efficacy of the GL67 lipid.

This lack of balance is somewhat disturbing, and it may be partially explained by the fact that the chapter author is the scientific director of gene transfer research at Genzyme. There is no disclaimer that the author is a paid employee of the company and therefore has a potential for conflict of interest. It is now standard practice for peer-reviewed medical articles and reports from research seminars to state at the very beginning any relationship (including financial) the scientist has with an industry sponsor, to warn the audience of a potential bias, and such disclaimers should have been included.

I wondered how many of the other chapter authors are paid consultants to pharmaceutical companies and have a financial interest in developing certain vectors and genes treatments for lung disease. Another question is how many of the authors have themselves founded companies based on their discoveries and thus have potential for financial gain if their technology becomes the "most favored?" At this point I must give my disclaimer: I am a liposome researcher and I founded a biotechnology company, the main focus of which is the development of plasmid liposome complexes for genetic therapy to the lungs. And so how balanced will my review of this volume be? That is not a question I can answer, but the reader should at least know my bias and judge accordingly.

Developing a gene therapy requires enormous amounts of money, which, currently, only industry is willing to invest. The collaboration of industry and academia can achieve that balance of translational research (ie, the academician's goal of conducting hypothesis-driven research that has a direct pathway to clinical applications) and drug development (ie, industry's goal of bringing to market an effective and safe therapeutic agent that grabs the market share for a particular disease/indication) that will improve the quality of life for our patients. We just need to be honest about our scientific and fiscal biases.

The next section of the book focuses on using gene transfer as a tool to study lung disease pathogenesis. I was excited at the prospect of reading these chapters, because I envisioned that they would contain much information that was new to me, as this area has not gotten much attention in the gene therapy literature until rather recently. I was not disappointed.

The 3 chapters in this section were well written, informative, and balanced. In these chapters a case is made that transient expression of cytokines and growth factors could give us important information on the biologic and disease roles of those factors. Unfortunately, much of the information in these 3 chapters was repetitive.

Content overlap is a problem throughout the book and it occurs with mind-numbing frequency, as was particularly evident in the book's last section, which is on gene therapy for specific diseases, including gene therapy, cystic fibrosis, cancer of the respiratory system, alpha-1 antitrypsin deficiency, diseases of the pulmonary circulation, acute lung injury, and lung transplantation. The 2 chapters on cancer are outstanding; they are packed with information and provide very thorough and balanced discussions on the challenges of gene therapy for cancer and how those challenges might be addressed. The 3 chapters on cystic fibrosis are informative but exceedingly repetitious; the background information in these chapters is either repetitive or should have been presented many chapters earlier. For example, the basic description of adeno-viral vectors, adeno-associated virus vectors, retroviral vectors, and liposomes as gene delivery system are presented in Chapter 12 ("Strategies for Gene Therapy of Cystic Fibrosis"); the basic description of adeno-associated virus vectors is repeated in

Chapter 13 ("Use of Adeno-Associated Virus in the Treatment of Cystic Fibrosis"); and extensive details on liposomes are given in Chapter 14 ("Use of Liposomes in the Treatment of Cystic Fibrosis"). But those gene delivery systems were described extensively in Chapters 2–6. In addition, the clinical description of cystic fibrosis does not need to be repeated in each of these 3 chapters.

These chapters (as with others in this volume) should have been edited to remove the repetition. In many instances the chapter authors do not see each others' manuscripts, so it is up to the series editor to consolidate information and remove repetition, which is time-consuming, but had it been done, the book could easily have been shortened by one quarter and it could have been a much more cohesive and integrated work. It could be argued that the repetition allows one to read only the specific chapter of interest, but that defeats the purpose of this series. Several review articles have appeared in medical journals on the topics in this book (except perhaps for lung transplantation) but the purpose of combining the information in such a book is to make the whole greater than the sum of the parts. Unfortunately, that is not the case here.

Chapter 15, "Delivery of Genes Through the Lung Circulation," is one of the best in the book. It is short, succinct, and provides much new information. The next 3 chapters (on alpha-1 antitrypsin de-

ficiency, acute lung injury, and lung transplantation) each have extension sections on the basic description of viral and non-viral vectors—all of which should have been eliminated. Each of these chapters includes introductory comments on the disease of interest and well-rounded discussions on the particular challenges of using gene therapy for the diseases in question. In particular, the final chapter on lung transplantation provides an excellent discussion on the challenges and opportunities of gene therapy for transplantation.

In summary, this is a book written by scientists for scientists. To date not a single person has had a lung disease cured by gene therapy, and that possibility is still several years in the future. Thus, this monograph will not affect clinical practice. However, the story of gene therapy is fascinating and can provide insight into the challenges of medical discovery. Unfortunately, the storytelling in this monograph is not its strength, and this tome's place is as a reference manual for MD and PhD gene therapy scientists.

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