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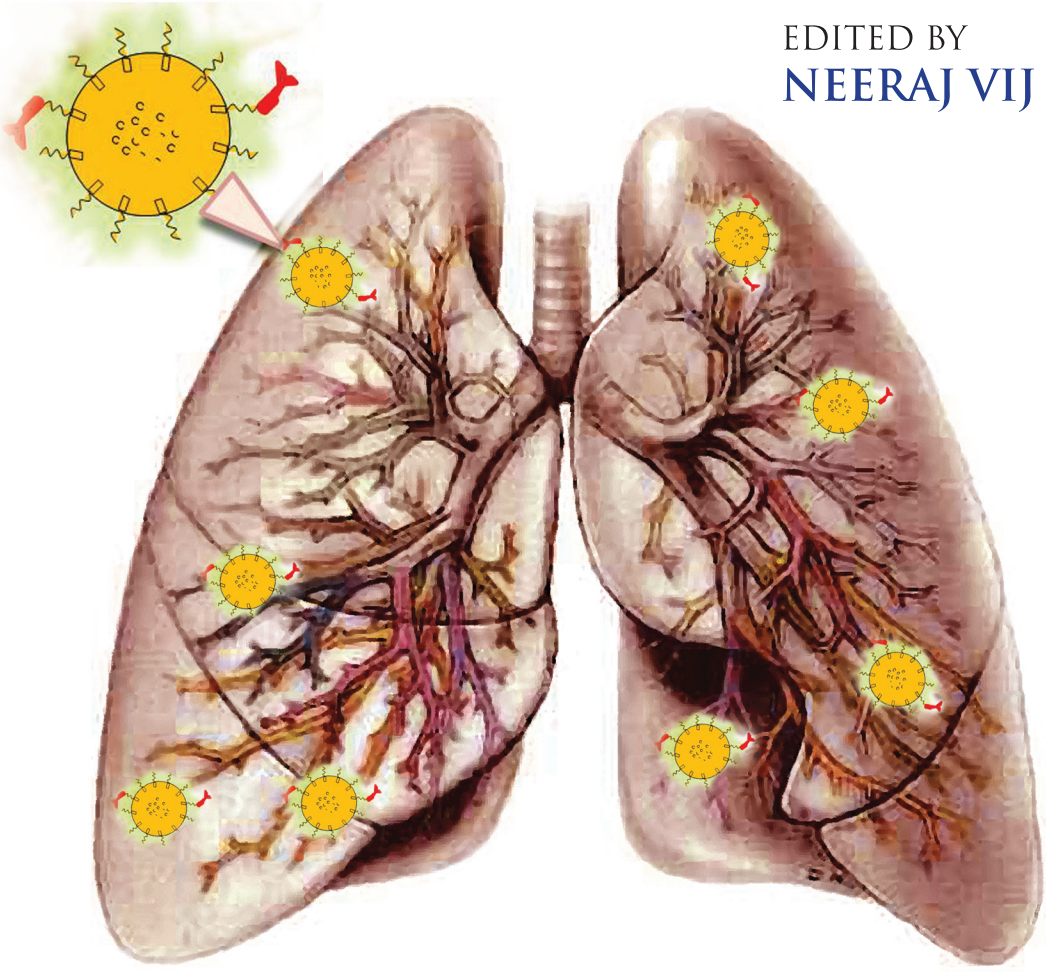
NEERAJ VIJ



PULMONARY NANOMEDICINE

DIAGNOSTICS, IMAGING, AND THERAPEUTICS

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To the fond memory of my parents,
who taught me to seek enlightenment and knowledge
and strive for excellence.

Dearest souls,
although you have departed and moved far away,
your perpetual memory in our hearts
makes us feel that you are ever near us, with us.

—N.V.

Contents

Contributors

James C. Bonner received his PhD in physiology from Mississippi State University in 1987, completed his postdoctoral training at the National Institute of Environmental Health Sciences (NIEHS) in 1990, and served as a principal investigator at NIEHS and at the Hamner Institutes for Health Sciences. He joined the Department of Environmental and Molecular Toxicology at NC State University as an associate professor in 2007.

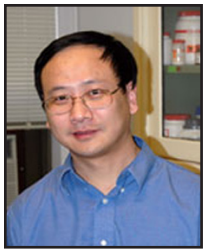
Dr. Bonner has over 20 years of experience in respiratory toxicology and lung disease pathogenesis. He has published more than 80 peer-reviewed research articles on environmental lung disease, numerous review articles, and several textbook chapters on respiratory toxicology.

He is the lead author of Chapter 9, on the potential respiratory health risks of engineered carbon nanotubes.

Aaron E. Foster received his BA in biology from the University of Puget Sound in Tacoma, Washington, in 1994 and his PhD in chemical engineering from the University of Sydney, Australia, in 2003. Currently, he is an assistant professor at the Center for Cell and Gene Therapy at Baylor College of Medicine.

Dr. Foster's research interests include cancer vaccine development, immune modulation, and gene therapy applications using cytotoxic T lymphocytes (CTLs) as anti-tumor effector cells or as carriers for *in vivo* delivery. In collaboration with Dr. Rebekah Drezek in the Department of Bioengineering at Rice University, he is also studying the development and use of multifunctional nanoparticles for the treatment of cancer and infectious disease.

Dr. Foster is the main author of Chapter 5, on the use of nanoparticles to treat airway inflammation.



Song Li received his MD in 1985 and PhD in tumor immunotherapy in 1991 from the Fourth Military Medical University, China. He worked with Dr. Leaf Huang at the University of Pittsburgh School of Medicine as a post-doc for two years and then as a research faculty for another four years. Dr. Li joined the faculty of the School of Pharmacy at the University of Pittsburgh in June 2000 and is currently an associate professor of pharmaceutical sciences. His major research interest is focused on the development of lipid- and polymer-based nanodelivery systems for targeted delivery of various types of therapeutics including nucleic acids (genes, siRNA, and peptide nucleic acids), proteins, and small molecules (e.g., anticancer agents and antioxidants).

Dr. Li is the main author of Chapter 7, on targeted delivery to the pulmonary endothelium.

Ashim K. Mitra received his PhD in pharmaceutical chemistry in 1983 from University of Kansas. He joined the University of Missouri–Kansas City in 1994 as chairman of Pharmaceutical Sciences. He is also vice provost for Interdisciplinary Research, Curators' Professor of Pharmacy, and director for Translational Research at University of Missouri–Kansas City, School of Medicine. Dr. Mitra has over 25 years of experience in ocular drug delivery and disposition and has authored or co-authored over 250 refereed articles and 30 book chapters in this field. He holds 8 patents and has made well over 450 presentations, including abstracts, at national and international scientific meetings. This work has attracted over 6 million dollars in funding from government agencies such as the National Institutes of Health (NIH) and Department of Defense (DOD) and from pharmaceutical companies.

Dr. Mitra is also a recipient of several research awards from AAPS, AACP, and various pharmaceutical organizations and serves on numerous editorial boards. According to Biomed Experts (during the past 10 years), he co-authored the third-highest number of publications in the world in the area of "Prodrugs." In April 2010, he was ranked fifth in the world among AAPS's Top Ten Researchers. In February 2012, his article "Ocular Drug Delivery" was again ranked as one of the top 5 downloaded articles in the *AAPS Journal*. Currently, he is chairman of the USP Council of Experts, General Chapter

<771> *Ophthalmic Preparations* Expert Panel, U.S. Pharmacopeia. His current research interests are focused on two main areas: delivery and targeting of antiviral agents and development of noninvasive delivery systems for peptide and protein drugs.

Dr. Mitra is the senior author of Chapter 3, which discusses the use of nasal and pulmonary delivery of macromolecules to treat respiratory and nonrespiratory diseases.

Shyam S. Mohapatra is a Distinguished USF Health Professor and director of the Division of Translational Medicine, Nanomedicine Research Center at the Morsani College of Medicine, University of South Florida. He also directs the Signature Program in Allergy, Immunology and Infectious Diseases at the college. A PhD graduate of the Australian National University, Prof. Mohapatra is a recipient of two international awards: the Alexander von Humboldt research fellowship (1984, Bonn, Germany) in genetics and Pharmacia Allergy Research Foundation Award (1992, Paris) for his contributions to the field of allergy and immunology.

Prof. Mohapatra's research program focuses on the molecular mechanisms underlying inflammation in respiratory diseases, cancers, viral infections, and traumatic brain injury. He has used nanotechnology approaches to advance translational research in these disease areas.

Prof. Mohapatra is the senior author of Chapter 6, which discusses the application of multifunctional chitosan nanocarriers in respiratory gene therapy.

Rajagopal Ramesh received his PhD in molecular biology in 1994 from the All India Institute of Medical Sciences, New Delhi, India. He completed his postdoctoral fellowships at Tulane University School of Medicine, New Orleans, in 1998 and later joined the faculty at M. D. Anderson Cancer Center in Houston, USA. Currently, Dr. Ramesh is a professor in the Department of Pathology and director of Experimental Therapeutics and Translational Cancer Medicine at the University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA. He holds the Jim and Christy Everest Endowed Chair in Cancer Developmental Therapeutics and the title of the Oklahoma TSET Cancer Research Scholar.

Dr. Ramesh's research is focused on investigating new cancer therapies with an emphasis on lung cancer. His laboratory has been conducting applied translational cancer research in leading areas such as cancer gene therapy, nanotechonology, and molecular targeted therapy. Research in his laboratory has led to four clinical trials for the treatment of cancer. He has published more than 86 articles in leading scientific journals and 17 textbook chapters on cancer therapy and drug development. His research is funded by the National Cancer Institute and other national granting agencies.

Dr. Ramesh is the senior author of Chapter 2, which discusses the use of multifunctional tumor-targeted nanoparticles for lung cancer.

Indrajit Roy received his MSc and PhD degrees from the University of Delhi, India, in 1997 and 2002, respectively. Following that, he completed postdoctoral research at the State University of New York (SUNY) at Buffalo, as well as at the Johns Hopkins School of Medicine. His research interests include the use of various nanoparticles for applications in targeted drug delivery, nonviral gene delivery, photodynamic therapy (PDT), and multimodal diagnostic imaging.

Dr. Roy has published more than 50 articles in leading scientific journals and holds 3 U.S. patents. In 2005, he was presented with the Visionary Innovator Award by the technology transfer office at SUNY, Buffalo. From 2005 to 2009, he served as a research assistant professor in the Institute for Lasers, Photonics and Biophotonics (ILPB) at SUNY, Buffalo. At present, he is an associate professor of chemistry at the University of Delhi.

Prof. Roy is the author of Chapter 4, on *in vitro* and *in vivo* diagnosis of pulmonary disorders using nanotechnology.

Venkataramana K. Sidhaye received her bachelor's in biomedical engineering in 1995 and her MD in 1998 at Northwestern University. She then did her residency in internal medicine and was a chief resident at Northwestern before coming to Johns Hopkins in 2002 for fellowship training in pulmonary and critical care medicine. She joined the Hopkins Pulmonary faculty in 2006. Dr. Sidhaye's research interest in is epithelial barrier function,

with a focus on the airway epithelium. She is interested in the cross-talk between the epithelial barrier and cell–cell contacts and the role of the epithelium in innate immunity, and this is modified by luminal exposures. More recently, she has been interested in epithelial responses to inspired nanomaterials.

Dr. Sidhaye is the senior and corresponding author of Chapter 8, on epithelial barrier targeting in chronic airway diseases.

Neeraj Vij received his PhD in biotechnology from the Indian Institute of Technology in 2001 and was also a recipient of international fellowship at the Institute of Genetics, Biological Research Center (Centre of Excellence of the European Union), Hungary, in same year. He subsequently completed his postdoctoral research at the University of Heidelberg, Germany, and The Johns Hopkins University School of Medicine (JHU SOM). Dr. Vij is currently an assistant professor at the Department of Pediatric Respiratory Sciences and Institute of NanoBiotechnology, JHU SOM. He serves on the editorial boards of several nanomedicine journals, including *Journal of Nanomedicine & Nanotechnology*, *Expert Opinion in Drug Delivery*, *International Journal of Nano Studies & Technologies*, and so forth. He has been invited to help organize several nanotechnology conferences and seminars, such as NanoBiotech 2009, and the nanotechnology postgraduate course at American Thoracic Society (ATS). He is also frequently invited to serve as a reviewer for various nanomedicine journals and grant review study sections, including NIH, USA. He is a life member of the American Society for Nano Medicine (ASNM) and several other international scientific societies. Dr. Vij has received several research awards and recognition for his scientific contributions.

The primary research focus of Dr. Vij's laboratory is identification of molecular pathways leading to chronic disease pathophysiology, with an aim to identify novel therapeutic sites. His laboratory is interested in applied and pre-clinical translational research and concentrates on the identification of novel therapeutic strategies including design and development of nano-based delivery systems for theranostic applications in chronic obstructive lung diseases.

Dr. Vij is the editor of this book and senior author of Chapter 1, which discusses the theranostic applications of nanotechnology in chronic obstructive lung diseases.

Preface

Nanotechnology has revolutionized medicine over the past decade. The unique physicochemical characteristics of engineered nanoparticles (ENPs) enable novel therapeutic and diagnostic (theranostic) applications, particularly in pulmonary diseases. The research over the past decade has provided insights into biological properties and application of NPs in pulmonary medicine.

This book provides a comprehensive review on the pulmonary applications of NPs and aims to enlighten the readers about novel nano-based theranostic strategies for treating pulmonary disorders. Each chapter discusses strategies to overcome the technological and disease-specific pathophysiological barriers to develop novel nano-based diagnostics, imaging, and therapeutic tools for treatment of various airway diseases.

In summary, the book is focused on emerging cutting-edge applications of nanotechnology in pulmonary medicine and aims to synchronize the efforts of pulmonary biologists, nano-chemists, and clinicians to develop novel nano-based theranostic systems for treatment of airway diseases.

This book has been compiled with the goal to serve both academic institutions and industry for education, training, and research. It is written to educate graduate and postgraduate students on emerging theranostic applications of ENPs in treating various pulmonary diseases. It will also serve as a guide for both clinicians and researchers in developing novel theranostics while closely monitoring the health effects of next-generation ENPs.

Overall, this is a wikipidea of pulmonary nanomedicine that discusses the scope of both current and future nanotechnologies for pulmonary applications.

Neeraj Vij, MS, PhD
Baltimore, MD
April 2012

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I express my sincere thanks to all authors and reviewers, who are experts in their respective fields, for their exceptional contribution and support. This book came into its present form with the earnest efforts of all authors, who helped me ensure that therapeutic and diagnostic strategies of novel pulmonary nanomedicine were discussed to help lead the advancement of the emerging scientific field of pulmonary nanomedicine. I am extremely grateful to Stanford Chong (Director) and Sarabjeet Garcha (Editorial Manager), of Pan Stanford Publishing Pte. Ltd., for their outstanding support and perceptiveness. Sarabjeet was especially instrumental in providing the much-needed editorial support for the swift collation of the book.

Neeraj Vij