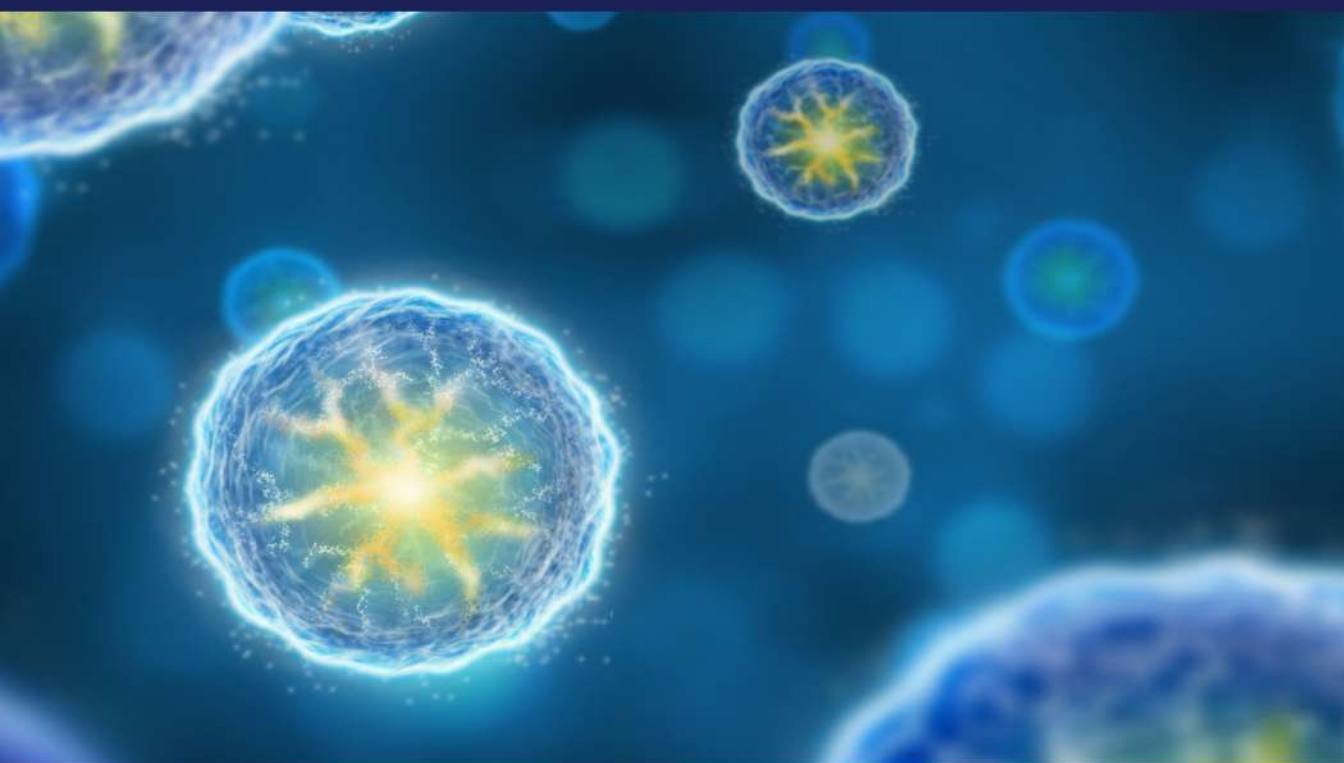


# EMERGING TRENDS IN **NANOBIOMEDICINE**

---

## NanoBioMaterials



**Bhupinder Singh  
Rodney J. Y. Ho  
Jagat R. Kanwar**



**CRC Press**  
Taylor & Francis Group

# NanoBioMaterials

Editor-in-Chief

**Bhupinder Singh**

Editors

**Rodney J. Y. Ho**

**Jagat R. Kanwar**



**CRC Press**

Taylor & Francis Group  
Boca Raton London New York

---

CRC Press is an imprint of the  
Taylor & Francis Group, an **informa** business

CRC Press  
Taylor & Francis Group  
6000 Broken Sound Parkway NW, Suite 300  
Boca Raton, FL 33487-2742

© 2018 by Taylor & Francis Group, LLC  
CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works

Printed on acid-free paper

International Standard Book Number-13: 978-0-8153-9978-0 (Hardback)  
International Standard Book Number-13: 978-1-351-13866-6 (eBook)

This book contains information obtained from authentic and highly regarded sources. Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, micro-filming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access [www.copyright.com](http://www.copyright.com) (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

**Trademark Notice:** Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

---

#### Library of Congress Cataloging-in-Publication Data

---

Names: Singh, Bhupinder, editor.  
Title: NanoBioMaterials / editor, Bhupinder Singh Bhoop.  
Other titles: NanoBioMaterials (Singh)  
Description: Boca Raton : Taylor & Francis, 2018. | Includes bibliographical references and index.  
Identifiers: LCCN 2018000548 | ISBN 9780815399780 (hardback : alk. paper) | ISBN 9781351138666 (ebook)  
Subjects: | MESH: Nanostructures--therapeutic use | Biocompatible Materials--therapeutic use | Drug Delivery Systems  
Classification: LCC R857.M3 | NLM QT 36.5 | DDC 610.28--dc23  
LC record available at <https://lccn.loc.gov/2018000548>

---

Visit the Taylor & Francis Web site at  
<http://www.taylorandfrancis.com>

and the CRC Press Web site at  
<http://www.crcpress.com>

---

# Contents

Foreword .....	vii
About the Series .....	ix
Preface.....	xiii
Editors .....	xv
Contributors .....	xvii
<b>Chapter 1</b> Applications of Nanostructured Biomaterials.....	1
<i>Shweta Sharma,* Ankush Parmar, and Surinder Kumar Mehta</i>	
<b>Chapter 2</b> Nanocoutured Metallic Biomaterials and Surface Functionalization of Titanium-Based Alloys for Medical Applications.....	17
<i>Jalal Azadmanjiri, Wai Hong Wong, Jagat R. Kanwar,* Christopher C. Berndt, James Wang, Vijay K. Srivastava, and Ajay Kapoor*</i>	
<b>Chapter 3</b> Graphene-Polymer Nanocomposites for Biomedical Applications.....	51
<i>Duo Wu, Mohammad Ramezani, and Minna Hakkarainen*</i>	
<b>Chapter 4</b> Lipid-Based Nanocarriers in Lymphatic Transport of Drugs: Retrospect and Prospects.....	67
<i>Vikas Rana,* Sunil Kamboj, and Sheshank Sethi</i>	
<b>Chapter 5</b> Nanocarriers in Early Diagnosis of Cancer .....	97
<i>Gurpal Singh,* Rajneet Kaur Khurana, Atul Jain, Taranvir Kaur, and Bhupinder Singh*</i>	
<b>Chapter 6</b> Dendrimers: Emerging Anti-Infective Nanomedicines .....	121
<i>Keerti Jain*</i>	
<b>Chapter 7</b> Production and Utilization of Nanofibers as Promising Biomaterials .....	139
<i>Yaser Dahman,* Valdir Mota Junior, Yan Xuan, Simon Nagy, Sumant Saini, Jasleen Kaur, and Bilal Khan</i>	
<b>Chapter 8</b> Fibro-Porous Composite Nanobiomaterials for Enhanced Biointegration.....	165
<i>Andrew T. Wood, Dominique T. Everett, Katelynne J. Herron, and Vinoy Thomas*</i>	
<b>Chapter 9</b> Nanocarrier-Mediated Therapeutic Protein Delivery .....	185
<i>Akhlesh Kumar Jain,* Teenu Sharma, and Sunil Kumar Jain</i>	

<b>Chapter 10</b>	Nanotechnology-Based Prodrug Conjugates for Site-Specific Antineoplastic Therapy .....	203
	<i>Nishi Mody, Rajeev Sharma, Surbhi Dubey, Atul Jain, and Suresh P. Vyas*</i>	
<b>Chapter 11</b>	Osteomyelitis: Therapeutic Management using Nanomedicines .....	221
	<i>Ashish Ranjan,* Teenu Sharma, Atul Jain, Sumant Saini, Shantanu Bandyopadhyay, Shreeniwas Singh, and Bhupinder Singh*</i>	
<b>Chapter 12</b>	Nanostructured Lipid Carrier-Mediated Methotrexate Delivery Evokes Transcription Factors to Induce Selective Apoptosis in Rheumatoid Arthritis .....	239
	<i>Naisargee Patel, Rajeev K. Tyagi,* and Neeraj K. Garg</i>	
<b>Chapter 13</b>	Superparamagnetic Iron Oxide Nanoparticles for Magnetic Hyperthermia Applications .....	247
	<i>Yogita Patil-Sen* and Vikesh Chhabria</i>	
<b>Chapter 14</b>	Development of In-House Nano-Hydroxyapatite Particles for Dental Applications ....	263
	<i>Sunpreet Singh and Rupinder Singh*</i>	
<b>Index</b> .....		277

---

# 9 Nanocarrier-Mediated Therapeutic Protein Delivery

*Akhlesh Kumar Jain, Teenu Sharma, and Sunil Kumar Jain\**

## CONTENTS

9.1	Introduction .....	185
9.2	Limitations and Challenges for Protein Delivery .....	186
9.3	Vesicular Nanocarriers .....	187
9.3.1	Liposomes .....	187
9.3.2	Niosomes .....	188
9.3.2.1	Protein and Peptide Delivery Using Niosomes .....	189
9.4	Particulate Carriers .....	189
9.4.1	Polymeric Nanoparticles .....	189
9.4.2	Solid Lipid Nanoparticles .....	193
9.4.2.1	Protein/Peptide-Loading in SLNs .....	193
9.5	Inorganic Nanocarriers .....	195
9.5.1	Silica Nanoparticles .....	195
9.5.2	Gold Nanoparticles .....	196
9.5.3	Calcium Phosphate Nanoparticles .....	196
9.6	Conclusions .....	197
	References .....	197

## 9.1 INTRODUCTION

Proteins are vital elements involved in all the essential activities of the biological system, such as signal transduction, enzyme catalysis, gene regulation and maintaining the classic balance of cell survival and programmed death (Walsh, 2010; Leader *et al.*, 2008). Advances in genetic engineering have led to proliferation in the enormous diversity of proteins with high biological purity. Despite their strength and specificity in physiological activities, most of the therapeutic proteins are tough to deliver clinically. Hence, an efficient means of transporting proteins to cells and organs of interest in an active state is a key aspect in tumor targeting, vaccination, regenerative medicine, treatment of functional loss and genetic disorders. Despite the administration of these peptides and proteins, these have very short biological half-life. The inherent problems to parenteral protein delivery are patient compliance, discomfort and high variability in bioavailability.

Noteworthy efforts in last decade have been carried out to synthesize nanoparticles (NPs) as delivery vehicles, since they provides appropriate ways of delivering low molecular weight therapeutics, as well as large bioactives, i.e. proteins, peptides, vaccines or nucleotides either by restricted or by tissue-specific delivery. Researchers, due to multiple reasons, are fascinated by nanocarriers as formulation vehicles, because the ratio of number of surface atoms or molecules to the total number of atoms or molecules is enhanced phenomenally, leading eventually to exponential augmentation of the effective surface area (Hadjipanayis *et al.*, 2010). Furthermore, nanocarriers can become much larger in number and, due to their tiny size, could reach regions of low accessibility such as tumor cells, damaged tissues and inflamed

---

\* Corresponding author.