



BIONANOTECHNOLOGY: NEXT-GENERATION THERAPEUTIC TOOLS

Editors:
Alaa A. Aljabali
Kaushik Pal

Bentham Books

Bionanotechnology: Next- Generation Therapeutic Tools

Edited by

Alaa A. Aljabali

*Department of Pharmaceutics and Pharmaceutical
Technology, Yarmouk University
Irbid 21163, Jordan*

&

Kaushik Pal

*Department of Physics University Centre for Research and
Development (UCRD)
Mohali, Gharuan, Punjab 140413
India*

Bionanotechnology: Next-Generation Therapeutic Tool

Editors: Alaa A. Aljabali, Kaushik Pal

ISBN (Online): 978-981-5051-27-8

ISBN (Print): 978-981-5051-28-5

ISBN (Paperback): 978-981-5051-29-2

© 2022, Bentham Books imprint.

Published by Bentham Science Publishers Pte. Ltd. Singapore. All Rights Reserved.

BENTHAM SCIENCE PUBLISHERS LTD.

End User License Agreement (for non-institutional, personal use)

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the ebook/echapter/ejournal (“**Work**”). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: permission@benthamscience.net.

Usage Rules:

1. All rights reserved: The Work is the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

Disclaimer:

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

Limitation of Liability:

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

General:

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of Singapore. Each party agrees that the courts of the state of Singapore shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.

80 Robinson Road #02-00

Singapore 068898

Singapore

Email: subscriptions@benthamscience.net



CONTENTS

PREFACE	i
LIST OF CONTRIBUTORS	ii
CHAPTER 1 AN OVERVIEW OF BIOMATERIAL TOXICITY AND EXCRETION	1
<i>Srijana Sharma, Yachana Mishra, Shubham Bisht, Neha Sharma and Vijay Mishra</i>	
INTRODUCTION	1
CHARACTERISTICS OF BIOMATERIALS	4
TYPES OF BIOMATERIALS	5
APPLICATIONS OF BIOMATERIALS	6
Tissue Engineering	6
Implantation of Medical Devices	7
Joint Prosthesis	8
Bone Repair	8
Drug Delivery Systems	9
TYPES OF TOXICITY	10
Hepatotoxicity	10
Nephrotoxicity	11
Cardiac Toxicity	12
Brain Toxicity	12
Lung Toxicity	13
MECHANISM OF TOXICITY	13
Cell Death	14
The Decline in Cell Adhesion	15
Alteration in Cellular Morphology	15
Cell Proliferation	16
FACTORS RESPONSIBLE FOR BIOMATERIAL TOXICITY	16
Particle Size	17
Morphology	18
Surface Charge	19
Coating	20
BIOPHARMACEUTICAL PROFILE OF BIOMATERIALS	21
Absorption	21
Distribution	21
Metabolism	22
Excretion	22
CONCLUSION	24
CONSENT FOR PUBLICATION	24
CONFLICT OF INTEREST	24
ACKNOWLEDGEMENT	24
REFERENCES	25
CHAPTER 2 NANO-BIOMATERIALS FOR IMMUNOTHERAPY APPLICATIONS	30
<i>Pooja Saxena</i>	
INTRODUCTION	31
IMMUNOTHERAPY & CANCER	32
ONCOLYTIC VIRUSES FOR IMMUNOTHERAPY	33
NON-REPLICATING VIRUSES FOR IMMUNOTHERAPY	35
VIRUS-LIKE PARTICLES FOR IMMUNOTHERAPY	37
EXTRA-CELLULAR VESICLES FOR IMMUNOTHERAPY	40

CONCLUSION	41
CONSENT FOR PUBLICATION	42
CONFLICT OF INTEREST	42
ACKNOWLEDGEMENT	42
REFERENCES	42
CHAPTER 3 LIPID-BASED NANOMATERIALS IN CANCER TREATMENT AND DIAGNOSIS	49
<i>Mohammad A. Obeid, Mohammed Al Qaraghuli, Marta Ruano, Sirikwan Sangboonruang, Manal Alsaadi, Hanin Alyamani, Yingmanee Tragoolpua and Valerie A. Ferro</i>	
CANCER BACKGROUND	50
NANOPARTICLE APPLICATIONS	51
TYPES OF LIPID-BASED NANOMATERIALS	53
Liposomes	53
Niosomes	54
Micelles	55
Solid Lipid Nanoparticles	55
METHODS OF PREPARATION OF LIPID-BASED NANOMATERIALS	56
High-energy Methodologies	56
<i>High-Pressure Homogenization (HPH) Method</i>	56
<i>High-speed Homogenisation</i>	57
<i>Ultrasonication</i>	57
Low-energy Methodologies	57
<i>Spontaneous Emulsification Method</i>	57
<i>Membrane Emulsification</i>	58
<i>Phase Inversion Temperature (PIT)</i>	58
<i>Coacervation</i>	58
<i>Double Emulsion Method</i>	58
<i>Methods Based on Using Organic Solvents to Stabilise pH- or Thermosensitive Drugs and Increase their Bioavailability</i>	59
<i>Methods Based on Supercritical Fluid</i>	59
Drying Methodologies	59
<i>Nano-spray-drying</i>	59
<i>Freeze-drying</i>	60
<i>Variosol</i>	60
CLINICAL APPLICATIONS OF LIPID-BASED NANOMATERIALS	60
CLINICALLY APPROVED LIPID-BASED NP MEDICINES	64
LIPID-BASED NANOMATERIALS IN DISEASES DIAGNOSIS	68
LIPID-NANOPARTICLES TOXICITY	70
CONCLUSIONS	71
CONSENT FOR PUBLICATION	71
CONFLICT OF INTEREST	71
ACKNOWLEDGEMENT	71
REFERENCES	71
CHAPTER 4 POLYMERIC NANOMATERIALS FOR CANCER THERANOSTICS	84
<i>Rajarshi Roychoudhury</i>	
INTRODUCTION	84
POLYMERIC NANOMATERIALS IN CANCER THERAPY	85
Delivery of Chemotherapeutics	85
Delivery of Genetic Material	87

Delivery of Diagnostics	87
POLYMERS USED FOR DELIVERY OF THERANOSTICS	88
NATURAL POLYMERS	89
Chitosan	89
Dextran	89
Alginate	90
Gelatin	90
Poly (L-Lysine)	91
SYNTHETIC POLYMERS	91
Poly (lactic-co-glycolic acid) (PLGA)	91
Cyclodextrins	91
Polyethyleneimine (PEI)	91
Poly (β -amino ester)	92
CONCLUDING REMARKS	92
CONSENT FOR PUBLICATION	92
CONFLICT OF INTEREST	92
ACKNOWLEDGEMENTS	92
REFERENCES	92
CHAPTER 5 MAGNETIC NANOPARTICLES FOR IMAGING, DIAGNOSIS, AND DRUG- DELIVERY APPLICATIONS	98
<i>Ejlal Abu-El-Rub, Hana M. Zegallai, Basma Milad Aloud, Saravanan Sekaran and Donald W. Miller</i>	
INTRODUCTION	99
General Features of MNPs	99
Physico-chemical Properties Influencing MNP Tissue Distribution	101
Magnetic Nanoparticles as Imaging Agents	102
MNPs as Molecular Imaging Agents	103
MAGNETIC NANOPARTICLES (MNPS) AS DIAGNOSTIC AGENTS	105
MAGNETIC NANOPARTICLES (MNPS) AND STEM CELLS	106
Use of MNPs for Labeling and Tracking Stem Cells	106
Guidance and Homing of Stem Cells	108
Improving Differentiation and Stem Cell Survival	110
MAGNETIC NANOPARTICLES FOR DRUG DELIVERY AND GENE THERAPY	111
MNPs in Respiratory Drug Delivery	111
MNPs in Ocular Drug Delivery	112
MNPs in Neurological Disorders	113
MNPs in Gene Therapy	114
MNPs in Cancer Therapy	115
CONCLUSION	117
CONSENT FOR PUBLICATION	118
CONFLICT OF INTEREST	118
ACKNOWLEDGEMENT	118
REFERENCES	118
CHAPTER 6 APTAMERS IN THERANOSTIC BIONANOMATERIALS	130
<i>Hamdi Nsairat, Walhan Alshaer, Ismail Sami Mahmoud, Mohammad A Ismail, Ezaldeen Esawi Shrouq Alsotari and Said I. Ismail</i>	
INTRODUCTION	130
APTAMERS	131
SELEX	133
APPLICATIONS OF APTAMERS	134

Diagnosis	134
Therapy	135
APTAMERS TARGETING FOR THERANOSTICS BIONANOMATERIALS	136
Targeted Delivery and Imaging of Anthracycline Nanomaterials	136
Targeted Delivery and Imaging of Taxane Nanomaterials	142
Targeted Delivery and Imaging of Nucleic Acid Drugs Nanomaterials	142
Targeted Delivery, Imaging, and Photodynamic Therapy (PDT)	143
Targeted delivery, imaging, and Photothermal therapy (PTT)	144
Other Targeted Drug Delivery and Multimodal Imaging	147
CONCLUSION	151
CONSENT FOR PUBLICATION	152
CONFLICT OF INTEREST	152
ACKNOWLEDGEMENT	152
REFERENCES	152
CHAPTER 7 VIRAL AND NON-VIRAL NANOPARTICLES FOR GENE THERAPEUTICS	159
<i>Hassan Elsana and Amal Ali Elkordy</i>	
INTERNAL AND EXTERNAL BARRIERS TO GENE THERAPY	159
GENE DELIVERY METHODS	161
Gene Delivery Using Viral Vectors	162
Direct Injection of Plasmid DNA	164
Chemical Based Vectors	165
<i>Lipid-Based Gene Delivery Carriers</i>	165
<i>Cationic Polymers</i>	167
<i>Inorganic Particles</i>	169
CELL TARGETING	171
Active Targeting	171
Passive Targeting	171
POTENTIAL TOXICITY OF NANOPARTICLES	171
CONCLUSION	172
CONSENT FOR PUBLICATION	172
CONFLICT OF INTEREST	172
ACKNOWLEDGEMENT	172
REFERENCES	172
CHAPTER 8 CONCLUSION, OUTLOOK, AND PROSPECTS: BIONANOMATERIALS IN	
CLINICAL UTILIZATION	177
<i>Alaa A A Aljabali, Kaushik Pal, Rasha M. Bashatwah and Murtaza M. Tambuwala</i>	177
INTRODUCTION	178
ADVANTAGES OF NANOBIO TECHNOLOGY	179
Applications of Nanobiotechnology in the Biomedical Field	179
Biopharmaceuticals	185
PROSPECTS OF NANOBIO TECHNOLOGY	185
ADVANTAGES OF NANOBIO TECHNOLOGY	188
CHALLENGES FOR NANOBIO TECHNOLOGY	188
POTENTIAL HAZARDS OF NANOPARTICLES	189
CONCLUSION	190
CONSENT FOR PUBLICATION	191
CONFLICT OF INTEREST	191
ACKNOWLEDGEMENTS	191
REFERENCES	191
SUBJECT INDEX	397

PREFACE

This book describes the design and characterization of bionanomaterials, which exhibit distinctive physical, chemical, and biological properties, and discusses how these functional nanomaterials enable the precise manipulation of the architectural, physical, and biochemical cellular environment *in vitro* and *in vivo*. Besides, it covers how they can act as carriers of diagnostic or therapeutic agents, thus providing new pathways or strategies for disease diagnosis and treatment. Specific chapters discuss protein delivery, drug delivery, tissue regeneration, bioimaging, bio-detection, molecular imaging, nucleic acid therapeutics, and DNA-based nanomaterials.

Furthermore, the book focuses on a unique subset of nanomaterials originating from biological entities and explores their potential as nanomedicine tools for selective drug delivery and molecular imaging. Bionanomaterials hold great potential as naturally occurring nanomaterials with enhanced properties, such as biodegradable, biocompatible, safety, and amenability for chemical and genetic manipulation to impart new surface functionalities for the selective targeting. Subsequently, such nanomaterials will enhance the therapeutics payload delivered selectively to the diseased cells. Besides, nanomaterials should have a higher signal-to-noise ratio, making them ideal as molecular imaging tools. Bionanomaterials can be produced in larger quantities at low cost, and most importantly, they are highly monodisperse, making them ideal candidates as tools in nanomedicine. Their composition in terms of chemical and structural point of view is unmatched to their synthetic counterparts, and as they comprise natural amino acids or natural monomers, they are safe and hold no side effects for the development as tools in nanomedicine and drug delivery.

The book series will be an international collaboration to present a comprehensive overview of bionanomaterials from natural sources and explore their benefits, advantages, and disadvantages compared to their synthetic counterparts. It will mainly help in practical academic research innovations in the areas of bionanomaterials. Furthermore, this book will explore the clinical demand for a subset material comprised of natural sources for advanced applications. The book is directed toward researchers, academics, and higher education students working on bionanomaterials in medical, pharmaceutical, environmental applications.

Alaa A. A. Aljabali

Department of Pharmaceutics and Pharmaceutical Technology
Yarmouk University, Faculty of Pharmacy
Irbid
Jordan

&

Kaushik Pal

Department of Physics
University Centre for Research and Development (UCRD)
Mohali, Gharuan, Punjab 140413
India

List of Contributors

- Alaa A A Aljabali** Faculty of Pharmacy, Department of Pharmaceutics and Pharmaceutical Technology, Yarmouk University, Shafiq Irshidat Street, Irbid 21163 - P. O. BOX-566, Jordan
- Amal Ali Elkordy** School of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences and Wellbeing, University of Sunderland, Sunderland SR1 3SD, UK
- Basma Milad Aloud** Department of Physiology and Pathophysiology, University of Manitoba, Winnipeg, Canada
- Donald W. Miller** Kleysen Institute for Advanced Medicine, University of Manitoba, Winnipeg, Canada
- Ejlal Abu-El-Rub** Department of Basic Medical Sciences, Faculty of Medicine, Yarmouk University, Irbid, Jordan
Department of Physiology and Pathophysiology, University of Manitoba, Winnipeg, Canada
- Ezaldeen Esawi** Faculty of Medicine, The University of Jordan, Amman 11942, Jordan
- Hana M. Zegallai** Department of Pharmacology & Therapeutics, University of Manitoba, Winnipeg, Canada
DREAM, Children's Hospital Research Institute of Manitoba, Winnipeg, MB, Canada
- Hanin Alyamani** Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, G4 0RE Glasgow, United Kingdom
- Hamdi Nsairat** Pharmacological and Diagnostic Research Center, Faculty of Pharmacy, Al-Ahliyya Amman University, Amman 19328, Jordan
- Hassan Elsana** School of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences and Wellbeing, University of Sunderland, Sunderland SR1 3SD, UK
- Ismail Sami Mahmoud** Department of Medical Laboratory Sciences, The Hashemite University, Zarqa, 13133, Jordan
- Kaushik Pal** Federal University of Rio de Janeiro, Cidade Universitaria, Rio de Janeiro, 21941-901, Brazil
- Manal Alsaadi** Department of Industrial Pharmacy, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya
- Murtaza M. Tambuwala** SAAD Centre for Pharmacy and Diabetes, School of Pharmacy and Pharmaceutical Science Ulster University, Coleraine, UK
- Marta Ruano** Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, G4 0RE Glasgow, United Kingdom
- Mohammad A Ismail** Faculty of Medicine, The University of Jordan, Amman 11942, Jordan
- Mohammad A. Obeid** Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Yarmouk University, Irbid, Jordan

- Mohammed Al Qaraghuli** Department of Chemical and Process Engineering, University of Strathclyde, 75 Montrose Street, Glasgow, G1 1XJ Glasgow, United Kingdom
Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, G4 0RE Glasgow, United Kingdom
Basra University College of Science and Technology, Al-Wofod street, Basra, Iraq
- Neha Sharma** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India
Rayat Institute of Pharmacy, Railmajra, Shaheed Bhagat Singh Nagar, (Punjab), India
- Pooja Saxena** Medicago R&D Inc., 1020 Route de l'Eglise, Quebec City, Quebec, G1V 3V9, Canada
- Rajarshi Roychoudhury** enGene Inc, 7171 Frederick Banting, Saint-Laurent, QC H4S 1Z9, Canada
- Rasha M. Bashatwah** Faculty of Pharmacy, Department of Pharmaceutics and Pharmaceutical Technology, Yarmouk University, Shafiq Irshidat Street, Irbid 21163 - P. O. BOX-566, Jordan
- Said I. Ismail** Faculty of Medicine, The University of Jordan, Amman 11942, Jordan
Qatar Genome Project, Qatar Foundation, Doha, Qatar
- Saravanan Sekaran** Department of Biotechnology, School of Chemical and Biotechnology, SASTRA Deemed to be University, Thanjavur- 613401, Tamil Nadu, India
Department of Pharmacology, Saveetha Dental college and Hospital, Saveetha Institute of Medical and Technical sciences (SIMATS), Chennai 600 007, Tamil Nadu, India
- Shrouq Alstori** Cell Therapy Center, The University of Jordan, Amman 11942, Jordan
- Shubham Bisht** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India
- Sirikwan Sangboonruang** Biotechnology section, Graduate School, Chiang Mai University, Chiang Mai, Thailand, 50200
- Srijana Sharma** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India
- Valerie A. Ferro** Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, G4 0RE Glasgow, United Kingdom
- Vijay Mishra** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India
- Walhan Alshaer** Cell Therapy Center, The University of Jordan, Amman 11942, Jordan
- Yachana Mishra** Department of Zoology, Shri Shakti Degree College, Sankhahari, Ghatampur, Kanpur Nagar (Uttar Pradesh), India
- Yingmanee Tragoolpua** Division of Microbiology, Department of Biology, Faculty of Sciences, Chiang Mai University, Chiang Mai, Thailand, 50200

CHAPTER 1

An Overview of Biomaterial Toxicity and Excretion

Srijana Sharma¹, Yachana Mishra², Shubham Bisht¹, Neha Sharma^{1,3} and Vijay Mishra^{1,*}

¹ School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India

² Department of Zoology, Shri Shakti Degree College, Sankhahari, Ghatampur, Kanpur Nagar (Uttar Pradesh), India

³ Rayat Institute of Pharmacy, Railmajra, Shaheed Bhagat Singh Nagar, (Punjab), India

Abstract: Biomaterial is a growing family of materials with specific physicochemical properties. Significant studies have been made to characterize the potential *in vivo* and *in vitro* toxicity of biomaterials. The cytotoxicity may be attributed to variations in the physicochemical properties, target cell types, particle dispersion methods, *etc.* The reported cytotoxicity effects mainly include the impact on the biological system and organ-specific toxicity such as CNS toxicity, lung toxicity, cardiac toxicity, dermal toxicity, gastrointestinal toxicity, *etc.* Despite cellular toxicity, the immunological effects of biomaterials, such as the activation of pulmonary macrophages and associated inflammation, have been extensively studied. In this chapter, the latest research results on the toxicological profiles of nanomaterials, highlighting both the cellular toxicities and the immunological effects, have been incorporated. This analysis also offers details on the overall status, patterns, and research needs for dealing with the toxicological behavior of biomaterials.

Keywords: Biomaterials, Cytotoxicity, Nanocarriers, Toxicity.

INTRODUCTION

With the development of human civilization, biomaterials evolved by incorporating various materials on various lengths from nano- to micro- to macro level with a simple focus on extending human life and improving quality of life. More than 1000 years ago, silver, in various ways, was used as an antimicrobial agent to prevent infection. Different surgical procedures can be found at the very beginning of civilization. However, perhaps the most significant development took place in biomaterials in 1901-2000. Over the past 60 years, the quality of life

* **Corresponding author Vijay Mishra:** School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), 144411, India E-mail: vijaymishra2@gmail.com

for millions of people has been improved through artificial limbs. Regenerative sutures have simplified surgical procedures, and various cardiac devices have saved lives. The advent of tissue engineering and organ rehabilitation pushes science limits today to make 2001-2100 the most exciting years in the biological field.

The term biomaterial describes something derived from biological sources, and it also describes substances that can be used in the human body as a machine. Polymer science took birth with medicinal polymers in the past, and research continues to expand the performance and stability of these components *in vivo*. Biomaterials are needed in clinical practice as a vital part of permanent implants like large blood vessels, waist implants, catheters, *etc.* In surgery, the early use of polymers has mainly focused on the evolution of connective tissue. Many new systems are emerging due to significant advances in the development and molecular cell biology. The drugs based on lots of unique nucleic acid and protein, which are not administered in the form of pills, provide the impetus for new polymers that can be incorporated to control the delivery of drug and genetic treatment. Tissue engineering has new applications that are integrated with physical requirements where the biomaterials assist the regeneration of body limbs and tissues [1].

Various polymers are utilized in several environmental programs, including polyethylene etherketone (PEK), polysulfone (PS), Silicone (SR), polyethylene terephthalate (PET), polymethylmethacrylate (PMMA), polyacetal (PA), polytetrafluoroethylene (PTFE), polyurethane (PU), polyethylene (PE). The most common composite polymer biomaterials are CF, carbon fiber/ultra-high molecular weight polyethylene (CF/UHMWPE), carbon fiber/epoxy (CF/epoxy), silica/SR, and HA/PE. Polymer materials are used for medicinal applications. Application in various disciplines has been received by polymers, such as tissue engineering, orthopedics, implants, dentistry, ophthalmology, and many other medical fields. Delivery programs designed for polymer enable the slow release of the drug from the body.

An investigation on the use of polymer in genetic therapy has been done. They show safer genetic predisposition as compared to viruses and vectors. Synthetic polymeric materials are widely used for biosensors, experienced devices, and biocontrols. Polymeric essentials should be made biocompatible for biomedical applications. Many of the polymeric systems utilized in the body for medical devices are termed biocompatible, whereas collagen encapsulation after implantation separates them from the body tissues. Polymeric implants may be considered biocompatible if they do not cause adverse responses. When polymers interact with blood cells, a thrombus is generated rapidly. Therefore, items with

blood adhesions that are non-thrombogenic should be utilized for bloodstream contact. Properly balanced polymers employed in treatments should detect and interact harmoniously with living cell components without unspecified interactions. Non-toxic biomaterials are used in various medical and surgical applications. During the growing phase, NDB'S are meant to degrade the body.

Polymers that can be natural or manufactured can be decomposed. The benefits offered by the latter are more significant than the first since they may be flexibly adapted to produce the required property portfolio. Synthetic polymers provide a dependable and immunogenic supply of materials. The standard method includes mechanical characteristics (friction, density, and cutting) and the breakdown time necessary for a given system as a common technique for selecting a polymer to be used as a biomaterial. After completing its goal, it should be lowered to the planting area, leaving non-toxic products. Important issues to consider here are additional biomaterial properties, such as land charge, polarity, distribution of active chemical groups, hydrophobicity, and hydrophilicity (or wettability). It is important to blend polymers with hydrolytically unstable reinforcement for biological control. Esters, anhydrides, orthoesters, and amides are the most active chemical groups [2].

Any synthetic or natural compound except drug, which treats, enhances, or alters muscle or organ function, is called a biomaterial. The most challenging issue to deal with is biomaterial selection due to its biological compatibility and needs. In recent years, material designers have shown much interest. The discovery of different polymers has significantly influenced the growth and control technologies in the tissue engineering industry. However, operators must guarantee that polymer-based biomaterials have long-term strength and dependability to be effective. Utilizing biomedical composite polymer materials gives numerous new choices and design options. Composites composed of polymers can gain several mechanical and biological characteristics that significantly enhance numerous biological applications.

Nevertheless, the manufacturing and marketing of partial or complete medical instruments built from compounds have begun in relatively few situations. Biocompatibility is an essential condition that all living things must meet. The medical study investigates new scientific obstacles to cell/genetic diagnosis, treatment, and prevention. Destroyed biomaterials change over time as the biomaterials undergo mass and surface degradation, leading to changes in the material's surrounding area. Non-corrosive materials also experience changes in chemical and structural properties. However, these changes are not so significant, and the time involved in the physical and chemical changes is much longer than in organic matter [3].

Nano-Biomaterials for Immunotherapy Applications

Pooja Saxena^{1*}

¹ Medicago R&D Inc., Canada 1020 Route de l'Eglise, Quebec City, Quebec G1V 3V9, Canada

Abstract: Because of their nano-size, biological compatibility, and ability to precisely engineer antigens displayed, payloads packaged, and destinations targeted, nano-biomaterials are gaining traction as next-generation therapeutic tools. Oncolytic viruses were the first to be exploited in cancer immunotherapy because these are natural cell killers and, in some cases, highly selective for cancerous cells. Further, oncolytic viruses can be engineered to encode immune-stimulators and therapeutic genes. However, for oncolytic viruses to work, it is essential to develop these as viable viruses with the ability to infect. This raises safety concerns and poses hurdles in regulatory approval. To circumvent this limitation, non-replicating viruses and virus-like particles have been explored for immunotherapeutic applications. The advantage of these is their inability to infect mammals, thereby eliminating bio-safety concerns. Nonetheless, concerns related to toxicity need to be addressed in each case. Several virus-like particle candidates are currently in preclinical development stages and show promise for clinical use *via* intertumoral administration, also referred to as vaccination *in situ*. In cases where *in situ* administration is not possible due to the absence of solid tumours or inaccessibility of the tumour, nano-biomaterials for systemic administration are desired, and extracellular vesicles fit this bill. Exosomes, in particular, can provide controlled abscopal effects – a property desirable for the treatment of metastatic cancer. This chapter discusses the state-of-the-art in the development of nano-biomaterials for immunotherapy. With a plethora of candidates in development and over two hundred clinical trials ongoing worldwide, nanobiomaterials hold great promise as effective cancer immunotherapies with minimal side effects.

Keywords: Adenovirus, AAV, Cancer vaccines, Checkpoint inhibitors, CPMV, Exosomes, Gene therapy, Immune suppression, Immunotherapy, *In-situ* vaccine, Nanoparticle, Oncolytic virus, Tumour micro-environment, Tumour remission, T-VEC, VLP, Virus-like particle.

* Corresponding author Pooja Saxena: Medicago R&D Inc., Canada 1020 Route de l'Eglise, Quebec City, Quebec G1V 3V9, Canada; Tell:001 418-658-9393; E-mail: pooja.jic@gmail.com

INTRODUCTION

Immunotherapy warrants the use of tools that stimulate or boost the natural defenses of a patient's immune system to treat or prevent disease. Traditionally, the term was coined to represent treatments for cancer that relied on boosting cellular immune responses, as with T-cell therapy, or manipulating immune regulation, as with checkpoint inhibitors [1]. However, with the world grappling with a pandemic in 2020 and with the realization that boosting one's immune responses is an effective way to fight a coronavirus infection [2, 3], immunotherapy is now used in the broadest sense for all immune-boosting treatments for infectious diseases and oncology. A significant advantage of cancer immunotherapy for the treatment of cancer over traditional methods is that it treats primary tumour as well as prevents metastasis and recurrence of tumours with few side effects. However, immunotherapy does not work for all patients and all cancers. Therefore, the success of an immunotherapeutic drug in a clinical trial depends immensely on patient selection. Even so, immunotherapy is most effective when supplemented with chemotherapeutic drugs or radiation [4].

Although a new and upcoming field, recent successes in immunotherapy have been catapulted by the application of nanobiomaterials for the administration of immunotherapy. Nanobiomaterials are often the immunotherapeutic agent themselves or a carrier of one. Nanobiomaterials can also lead to activation of immune responses in the tumour micro-environment in case of solid tumours allowing the destruction of cancer cells and cancer remission [5, 6]. Apart from the obvious advantages of nano-size and biocompatibility, what makes nanobiomaterials ideal for immunotherapy applications is their amenability [7 - 10]. Using the knowledge available on structure at the atomic level, as in the case of viruses, engineering is possible to precisely display antigens on the nanoparticle exterior [11, 12]. In parallel, using molecular biology tools for genome engineering, it is possible to introduce functional genes within the nanoparticles to orchestrate immune responses. Moreover, space available within the nanoparticle can be exploited for packaging therapeutics [13, 14] such as drugs or genes or siRNA for delivery either by *in situ* administration at the tumour site or targeted systemic administration [8]. In both cases, side effects are limited. This is a significant advantage over conventional chemotherapy, where side-effects to healthy dividing cells, such as hair follicles, digestive tract, and blood-forming cells, are common [15].

Since the advent of the field of nanotechnology in 1959 by Richard Feynman [16], nanomaterials have been extensively used in material sciences and biotechnology. This chapter focuses on different classes of nanomaterials with applications in immunotherapy. The term nanobiomaterial is used for any nano-

scale product of biological origin, *i.e.*, mother nature's own nanoparticle toolkit. Several non-biological nanomaterials are also being developed as immunotherapies with significant promise. These include synthetic polymeric nanoparticles [17], liposomes [18], antigens [19] and peptides [20]. However, these will not be discussed in this chapter. A pictorial depiction of all the nanoparticles discussed in this chapter is presented in Fig. (1).

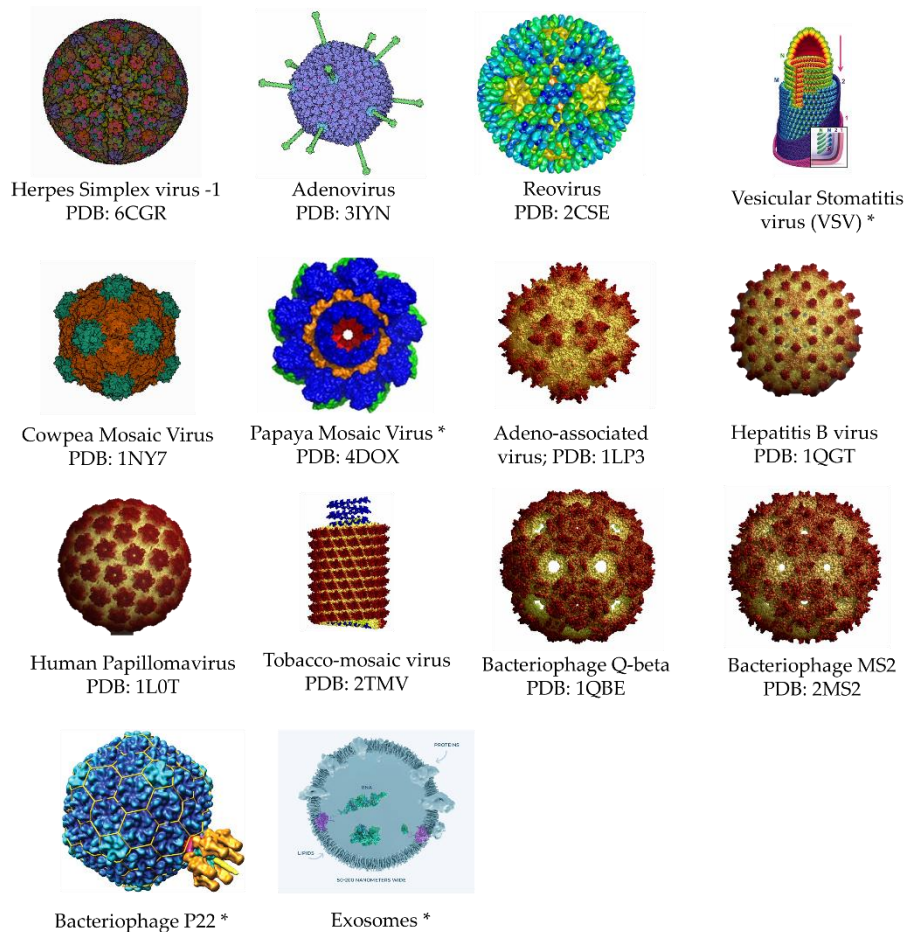


Fig. (1). A pictorial representation of all the nanoparticles discussed in this chapter, in order of their mention. Images are not to scale. Images were acquired from the Protein Data Bank [21] where available and the PDB identification number for each is mentioned in parentheses. Images not obtained from PDB have been marked with an asterisk and duly cited [22 - 25].

IMMUNOTHERAPY & CANCER

This section is intended for those who are not familiar with immunotherapy as it is imperative that immunotherapy concepts are understood to be able to grasp the

CHAPTER 3

Lipid-Based Nanomaterials in Cancer Treatment and Diagnosis

Mohammad A. Obeid^{1,*}, Mohammed Al Qaraghuli^{2,3,4}, Marta Ruano³, Sirikwan Sangboonruang⁵, Manal Alsaadi⁶, Hanin Alyamani³, Yingmanee Tragoolpua⁷ and Valerie A. Ferro³

¹ Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Yarmouk University, Irbid, Jordan.

² Department of Chemical and Process Engineering, University of Strathclyde, 75 Montrose Street, Glasgow, G1 1XJ Glasgow, United Kingdom.

³ Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 161 Cathedral Street, G4 0RE Glasgow, United Kingdom.

⁴ Basra University College of Science and Technology, Al-Wofod street, Basra, Iraq.

⁵ Biotechnology section, Graduate School, Chiang Mai University, Chiang Mai, Thailand, 50200.

⁶ Department of Industrial Pharmacy, Faculty of Pharmacy, University of Tripoli, Tripoli-Libya

⁷ Division of Microbiology, Department of Biology, Faculty of Sciences, Chiang Mai University, Chiang Mai, Thailand, 50200

Abstract: Cancer consists of a wide range of diseases that are mainly driven by the continuous unregulated proliferation of cancer cells. Current treatment options include the use of chemotherapies, radiotherapy, and surgery. Recently, there was an increased interest in applying nanoparticles (NPs) in cancer diagnosis and treatment. NPs are materials in the size range 1 to 100 nm and can be classified based on their properties, shape, or size. They have attracted wide attention because of their versatile physicochemical properties, nanoscale sizes, high surface-to-volume ratios, favourable drug release profiles, and targeting modifications. Nanotechnology can be used to improve the personalisation of cancer diagnosis and treatment by enhancing the detection of cancer-specific biomarkers, imaging of tumours and their metastases, specific drug delivery to target cells, and real-time observation of treatment progression. This chapter will highlight the main types of lipid NPs with their preparation methods. The clinical applications of these lipid NPs in cancer diagnosis and treatment will be presented along with the currently approved drugs based on these NPs.

* Corresponding author Mohammad A. Obeid: Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Yarmouk University, Irbid, Jordan; E-mail: m.obeid@yu.edu.jo

Keywords: Cancer diagnosis, Cancer treatment, Lipid nanoparticles, Liposomes, Micelles.

CANCER BACKGROUND

Cancer is considered one of the fatal diseases that has reported high incidence and mortality rates globally [1]. For instance, the Global Cancer Observatory (GLOBOCAN) 2020, an online database of global cancer statistics and estimates of occurrence and death rates in 185 countries for 36 types of cancer, has indicated that 19.3 million new cancer patients were diagnosed and around 10 million deaths caused by cancer in 2020 [1]. Therefore, interest in studying cancer continues to progress at a high rate to investigate the underlying causes of cancer and progression.

On a biological level, cancer consists of a wide range of diseases that are mainly driven by the continuous unregulated proliferation of cancer cells [2]. Over growth of cells may develop a mass of tissues called a tumour. However, tumours can be benign or malignant [3]. Benign tumours are usually non-invasive and can be removed without the risk of reoccurrence. Also, cells of benign tumours do not circulate or spread to other parts of the body [4]. At the same time, malignant tumours can invade nearby tissues and spread to other parts of the body in a process known as metastasis [4].

Cancer types are classified into five main categories according to their origin, for instance, carcinoma usually originating from epithelial cells, sarcoma arising from bone, cartilage, fat, muscle, blood vessels, leukemia from the bone marrow, while lymphoma and myeloma are found to be derived from cells of the immune system, and central nervous system cancers from brain tissues and spinal cord [2, 4]. Therefore, different types of cancer exhibit various behaviors and responses to treatment [2].

Cancer initiation and progression are viewed as a multi-step process at a cellular level, where progressive genetic alterations transform normal human cells into highly malignant ones. These genetic changes are found to affect three gene classes: proto-oncogenes, tumour suppressor genes, which are both involved in normal cell growth and division, and DNA repair genes that are responsible for fixing damaged DNA [2, 5]. For instance, any modifications, amplifications, or deletions in these genes may cause a de-coupling of normal cell growth and differentiation [5, 6]. Moreover, these changes in the cell's genetic material may arise unexpectedly or be induced by a factor or carcinogen that causes cancer [2].

Carcinogens include solar ultraviolet radiation, chemicals in tobacco smoke, and viruses. However, carcinogenesis, the process of cancer development, does not

rely only on single causes in most cancers. It has been found that many factors contribute to both animal models and humans [2].

However, preventive measures can be taken against some carcinogens such as radiation and smoking in order to minimise the incidence rate of cancer, as it has been found that more than half of all cancers are preventable [7]. However, integrating effective therapeutic approaches and developing new ones is limited [8].

In recent years, different forms of cancer have been effectively treated by immunotherapies such as antibodies [9], stem cell therapies [10], and chimeric antigen receptor (CAR)-T cell therapies [11, 12]. The success of these approaches is attributed to the high specificity and efficacy of these molecules in treating both primary and metastasised tumours. Despite the high promise of these approaches, a few undesired side effects can also arise, like autoimmune disease [13]. Furthermore, lymphoma and other non-solid tumours have generally shown better responses to immunotherapies than solid tumours [14, 15] due to the expected difficulty in penetrating solid tumours [16]. The immune-suppressive tumour microenvironment can similarly contribute to this efficacy reduction against solid tumours [17]. These limitations can be surpassed through the utilisation of nanotechnology.

NANOPARTICLE APPLICATIONS

Nanoparticles (NPs) are materials in size range 1 to 100 nm and can be classified based on their properties, shape, or size [18]. They have attracted wide attention because of their versatile physicochemical properties, nanoscale sizes, high surface-to-volume ratios, favourable drug release profiles, and targeting modifications [19, 20]. Nanotechnology can be used to improve personalisation of cancer diagnosis and treatment by enhancing the detection of cancer-specific biomarkers, imaging of tumours and their metastases, specific drug delivery to target cells, and real-time observation of treatment progression [21, 22].

The crucial challenge in treating cancer resides in engineering an effective treatment that targets cancer cells without affecting surrounding healthy cells [23]. The NPs must pass through several physiological and biological barriers to be effective. So their use as delivery systems inflicts necessities to optimise their size, surface chemistry, and biocompatibility to avoid non-specific interactions and enable specific binding to their targets. Attia *et al.* [24], specified different criteria that should be maintained by all therapeutic NPs, including the ability to remain stable in the blood and tumour microenvironment (TME); to evade reticuloendothelial system (RES) clearance, and prevent being seized by the mononuclear phagocyte system (MPS); to accumulate in tumour tissues through

Polymeric Nanomaterials for Cancer Theranostics

Rajarshi Roychoudhury^{1,*}

¹ enGene Inc., Canada 7171 Frederick Banting, Saint-Laurent, QC H4S 1Z9, Canada

Abstract: Despite global efforts for decades, the number of cancer cases is still on the rise. Although in recent times there has been significant improvement in immunotherapy, chemotherapy remains standard care for cancer patients alongside radiation and surgery. Chemotherapeutic drugs and diagnostic agents (MRI, PET, Ultrasound) lack specificity and often suffer from poor solubility and unwanted biodistribution. This results in unnecessary high dose requirements, systemic toxicity, and compromised quality of life for the patients. Beside therapy, early diagnosis is essential for the successful treatment and cure of cancer patients, just like any other disease. Therefore, a suitable delivery vehicle is always needed for the theranostic agents. Viral vectors are routinely used for the delivery of genetic material. But parallelly, nanoparticles made with biodegradable, non-toxic, and non-immunogenic polymers are often used as a carrier of chemotherapy drugs, diagnostic agents as well as genetic materials. Once decorated with specific ligands, these nanocontainers can deliver cargo molecules to target tissue and organs with high precision.

Keywords: Biodistribution, Cancer, Cargo, Cationic, Chemotherapy, Delivery, Diagnostic, Drug, Encapsulation, Gene, Hydrophobic, Hydrophilic, Immunotherapy, Ligand, Nanoparticle, Polymer, Receptor, Target, Toxicity, Systemic.

INTRODUCTION

Despite significant global efforts into the research and development of cancer therapeutics for decades, the number of cancer cases is expected to increase continuously. It has been estimated that there are currently 18.1 million new cancer cases every year, with 9.6 million deaths per year, accounting for 1 out of 6 deaths globally [1]. Cancer therapies are currently limited to surgery, radiation, and chemotherapy, with very few exceptions of immunotherapy (CAR-T or checkpoint inhibitors). All three methods risk damage to normal tissues or incomplete eradication of cancer. Beside surgery and therapy, a lot of emphasis also needs to be put on the diagnostics of cancer. Just like any other disease, if

* Corresponding author Rajarshi Roychoudhury: enGene Inc., Canada 7171 Frederick Banting, Saint-Laurent, QC H4S 1Z9, Canada; Tell:+1-514-332-4888; E-mail: rroychoudhury@engene.com

detected early enough, many types of cancer can be cured. Consequently, cancer therapy has become a multidisciplinary challenge requiring close collaboration among clinicians, biological and material scientists, and biomedical engineers.

Though chemotherapy is successful to some extent and remains standard of care for most cancers, the chemotherapy drugs lack specificity. Thus, in the process of killing cancer cells, they also damage healthy tissues leading to systemic toxicity and adverse side effects. It significantly affects the quality of life of the patient. Most chemotherapeutic drugs are administered *via* intravenous or oral route, which leads to rapid clearance and unwanted biodistribution of the drug. Therefore, chemotherapy drugs need to be administered in excess leading to unnecessary side effects [2]. That is why a vehicle with high specificity to cancer cells can circumvent the undesired systemic toxicity of the chemotherapeutic agents and other drugs.

Often that vehicle is a nanoparticle, either polymeric or protein-based. Nanoparticles are submicron-sized particles with diameters ranging from 10 to 1000 nm that can either encapsulate or display a cargo molecule of interest. These nanoparticles can also be decorated with receptor-specific ligands that can deliver the cargo molecule specifically to the desired tissue or organ, curtailing toxicity [3 - 5]. This book chapter discusses the application of polymeric nanoparticles as theragnostic in cancer.

POLYMERIC NANOMATERIALS IN CANCER THERAPY

Delivery of Chemotherapeutics

Every time any new cell is formed, it goes through a usual process to become a fully functioning (or mature) cell. The process involves a series of phases and is called the cell cycle. Chemotherapeutic drugs target cells at different phases of the cell cycle. Understanding how these drugs work helps doctors predict which drugs are likely to work well together. Doctors can also plan how often doses of each drug should be given based on the timing of the cell phases. Cancer cells tend to form new cells more quickly than normal cells, and this makes them a better target for chemotherapy drugs. However, chemo drugs cannot tell the difference between healthy cells and cancer cells. This means normal cells are damaged along with the cancer cells, and this causes side effects. Each time chemo is given, it means finding a balance between killing the cancer cells (to cure or control the disease) and sparing the normal cells (to lessen side effects). The good news is that most normal cells will recover from the effects of chemo over the time. But cancer cells are mutated (not normal) cells, and they usually do not recover from the effects of chemo. Therefore, chemotherapy is good at killing many types of cancer cells (Table 1).

Table 1. Different types of chemotherapeutic drugs and their mechanisms of action.

Types of Drugs	Mechanism of Action	Name of Few Drugs
Alkylating agents	Stops cell proliferation by DNA damage	Cisplatin, Busulfan, Oxaliplatin, Trabectedin
Antimetabolites	Interference with DNA and RNA by acting as a substitute for the normal building blocks of RNA and DNA.	5-fluorouracil, Capecitabine, Hydroxyurea, Thioguanine
Antitumor antibiotics	Altering DNA inside cancer cells to keep them from growing and multiplying.	Doxorubicin, Epirubicin, Idarubicin, Valrubicin
Topoisomerase inhibitor	Interference with topoisomerases	Irinotecan, Topotecan, Etoposide, Teniposide
Mitotic inhibitors	They work by stopping cells from dividing to form new cells	Paclitaxel, Docitaxel, Vinblastine, Vincristine

We will discuss one specific example of Paclitaxel. It is a microtubule-stabilizing agent that triggers polymerization of tubulin, killing cancer cells by disrupting the dynamics necessary for cell division. It has been found to be effective against a wide range of cancers, including head and neck, ovarian, lung, breast, and colon cancers. However, Paclitaxel is a highly hydrophobic drug with extremely low solubility in water and biological fluid (< 0.5 mg/L) [6, 7]. This drug on its own cannot be administered by intravenous injection as it can aggregate in blood vessels leading to embolization. It often shows local toxicity because of high drug concentrations at the site of deposition. This is why paclitaxel needs to be adequately formulated prior to administration.

The currently available formulation for paclitaxel includes the use of Cremophor EL (polyethoxylated castor oil) and dehydrated ethanol. Unfortunately, Cremophor EL is known to be toxic and can cause serious side effects [5]. Alternatively, surfactants could be used to solubilize the drug, but due to their high critical micellar concentration they cannot maintain the nanoparticle architecture. In this regard, thermodynamically stable polymeric micelles with a hydrophobic core and hydrophilic surface could serve as an effective delivery system for poorly soluble drugs [8 - 10].

The biodistribution of a given drug is a major factor for the success of chemotherapy. To minimize off-target toxicity and rapid clearance from the body, anticancer drugs must show sustained, controlled, and targeted release. In theory, these properties could be obtained by developing formulations that are controlled at the nanometer scale. For example, controlled and sustained drug release may be achieved by precisely adjusting the composition of nanoparticle formulations. Improved drug targeting ability could be obtained by functionalization of the

Magnetic Nanoparticles for Imaging, Diagnosis, and Drug-Delivery Applications

Ejlal Abu-El-Rub^{1,2}, Hana M. Zegallai^{3,4}, Basma Milad Aloud², Saravanan Sekaran^{5,6} and Donald W. Miller^{3,7,*}

¹ Department of Basic Medical Sciences, Faculty of Medicine, Yarmouk University, Irbid, Jordan

² Department of Physiology and Pathophysiology, University of Manitoba, Winnipeg, Canada

³ Department of Pharmacology & Therapeutics, University of Manitoba, Winnipeg, Canada

⁴ DREAM, Children's Hospital Research Institute of Manitoba, Winnipeg, MB, Canada

⁵ Department of Biotechnology, School of Chemical and Biotechnology, SASTRA Deemed to be University, Thanjavur-613401, Tamil Nadu, India.

⁶ Department of Pharmacology, Saveetha Dental college and Hospital, Saveetha Institute of Medical and Technical sciences (SIMATS), Chennai600 007, Tamil Nadu, India.

⁷ Kleysen Institute for Advanced Medicine, University of Manitoba, Winnipeg, Canada

Abstract: Magnetic Nanoparticles (MNPs) have gained interest within the research community due to their therapeutic potential in a variety of medical applications. MNPs are generally composed of a metallic core stabilized by the addition of an outer shell that can be further functionalized through the absorbance or conjugation of various targeting ligands. The magnetic properties of these nanoparticles can be utilized for imaging, localized drug delivery, and enhanced diagnostic detection. This chapter highlights the applications of MNPs to enhance magnetic resonance imaging (MRI) capabilities and improve the delivery of therapeutic agents to difficult-to-reach areas in the body. In addition, recent advances in the use of MNPs in stem cell therapy for both the tracking and monitoring of stem cell distribution in the body and improving engraftment and differentiation in stem cell therapy are discussed. Finally, examples of the incorporation of MNPs in diagnostic assays to improve rapid and real-time detection capabilities of many diseases, including cancer, cardiovascular diseases, and pathogen infections, are provided.

Keywords: Diagnostic agents, Drug delivery, Imaging agents, Magnetic Nanoparticles (MNPs), Stem cell therapy.

* **Corresponding author Donald W. Miller:** Department of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, MB, Canada and Kleysen Institute for Advanced Medicine, University of Manitoba, Winnipeg, Canada; E-mails: donald.miller@umanitoba.ca

INTRODUCTION

Magnetic nanoparticles (MNPs) are critical components in many biomedical applications. Although concerns regarding long-term safety remain to be addressed, MNPs are currently being explored in a variety of biomedical applications, including MRI imaging [1 - 3], bio-sensing diagnosis [1, 4], stem cell delivery, and tracking [5], gene therapy and drug delivery to treat multiple disorders including cancer, neurodegenerative diseases, HIV/AIDS, ocular diseases, and respiratory diseases [3, 6, 7]. Despite recent advances in nanomedicine using MNPs, there are many challenges to be solved in order to achieve optimal performance of these nanomaterials. The major limitations associated with MNPs include 1) development of synthesis schemes and storage and handling protocols that can be scaled-up for clinical applications while retaining necessary reproducibility in terms of size, charge, and surface properties [8, 9], 2) identification of the long-term toxicity of MNPs [9, 11], and 3) management of unexpected results due to biocompatibility and immunogenicity [9, 12].

While there are a variety of synthetic pathways and a multitude of different compositions, MNPs for medical applications all share the following common components; a magnetic core, a protective outer layer, and a surface that can be functionalized to improve targeting or biodistribution properties (Fig. 1) [13, 14]. Magnetic nanoparticles can be further classified as either ferromagnetic, paramagnetic, antiferromagnetic, diamagnetic, or ferrimagnetic based on their core material and resulting magnetic properties. Ferromagnetic nanoparticles consist of iron, nickel, or cobalt cores and display strong magnetic moments when placed in an external magnetic field. Ferrimagnetic nanoparticles have maghemite or magnetite iron oxide core material and display similar characteristics as ferromagnetic material in the presence of an external magnetic field. Paramagnetic materials have gadolinium, magnesium, and lithium as core materials. Magnetic nanoparticles formed from paramagnetic material have weaker magnetic moments and do not sustain their magnetic properties following the removal of the magnetic field, as observed with ferromagnetic materials. The MNPs formed from diamagnetic material commonly have copper, gold, or silver cores and have the weakest magnetic moments. The strong magnetic moments of the ferromagnetic and ferrimagnetic nanoparticles make them of interest for diagnostic agents, as well as in hyperthermia-based treatment applications.

General Features of MNPs

While many magnetic core materials are available for MNP synthesis, some, such as cobalt, chromium, and alkaline earth metals, used in ferromagnetic material, are toxic and cannot be used for biomedical applications unless being coated with

a safe, non-toxic protective layer [15, 16]. Thus, despite the strong magnetic moments inherent in these MNPs, the potential toxicity of these ferromagnetic materials has limited their use as imaging agents and therapeutics for animal and human applications. In contrast, the MNPs made with magnetite and maghemite iron-oxide as core material have established safety profiles that make them more suitable for imaging and diagnostic purposes [10, 17, 18].

Regardless of the magnetic core material used, the MNPs are typically coated with biocompatible materials to prevent corrosion or the leaching of the core [11, 19]. Silane-based coatings have been particularly useful for MNPs with iron oxide core material as they readily react with the core to form a protective silane shell that can be further modified for the particular application. The ability of silane-based coatings to retain the crystallinity of the metal oxide core preserves the magnetic properties while providing an outer shell that enhances the stability of the MNPs (*i.e.*, prevents aggregation), making them ideal surface components. The utility of the silane coatings as intermediates for further surface modifications is particularly attractive. This is illustrated in the studies of Yathindranath and coworkers [20]. Using aminosilane functionalization of iron oxide nanoparticles as intermediates, Yathindranath and coworkers demonstrated the utility of silane-based surface coatings properties to accommodate changes in surface charge, through variations in amide and carboxylic acid function groups, as well as hydrophobic/hydrophilic balance, through covalent attachment of oleic acid and albumin [20]. Silane-based coatings of iron oxide nanoparticles have shown favorable safety profiles in various models [21, 22] while providing flexibility for a multitude of different surface modifications.

In addition to the silane inorganic surface modifications other coatings have also been considered. Natural coatings consisting of carbohydrates, such as dextran and starch, or proteins such as albumin and various synthetic polymers have been used as surface coatings for MNPs [23, 24]. The natural polymer surface coatings are mostly hydrophilic and require cross-linking to prevent them from disassociating in aqueous environments and to enhance their mechanical strength. In contrast, commercially available synthetic polymers used for coating purposes such as poly (ethyleneglycol) (PEG) and polyvinyl alcohol (PVA) [25, 26] are hydrophobic and display improved mechanical strength over the hydrophilic coatings. Surface modifications of MNPs are important to ensure proper attachment of biomolecules and, in the case of drug delivery applications, to control release of drug at the target site [27]. Organic linkers such as carboxylic acid and aldehyde thiol allow for the attachment of biomolecules to a variety of functional groups on the surface of the MNPs [28, 29].

Aptamers in Theranostic Bionanomaterials

Hamdi Nsairat¹, Walhan Alshaer^{2,*}, Ismail Sami Mahmoud³, Mohammad A Ismail⁴, Ezaldeen Esawi⁴, Shrouq Alstori² and Said I. Ismail^{4,5}

¹ *Pharmacological and Diagnostic Research Center, Faculty of Pharmacy, Al-Ahliyya Amman University, Amman19328, Jordan*

² *Cell Therapy Center, The University of Jordan, Amman11942, Jordan*

³ *Department of Medical Laboratory Sciences, The Hashemite University, Zarqa, 13133, Jordan*

⁴ *Faculty of Medicine, The University of Jordan, Amman11942, Jordan*

⁵ *Qatar Genome Project, Qatar Foundation, Doha, Qatar*

Abstract: Theranostic nanomaterials hold the potential to revolutionize future disease management. Recent progress in nanomaterials technology and aptamer-based-targeting molecules have promoted efficient theranostics models. Aptamers are unique three-dimensional structures consisting of oligonucleotide (25-80 nt) polymers. They are comparable to monoclonal antibodies in their receptor-driven binding efficacy toward specific target receptors and binding ability to specific target molecules with high affinity and specificity. Aptamers have several other advantages, including prolonged shelf life, little or no variation from batch to batch, and ease of chemical modifications for enhanced stability and targeting capacity. Owing to the advantages mentioned above, aptamers are attracting great attention in diverse applications ranging from therapy, drug delivery, diagnosis, and functional genomics as well as biosensing. Herein, the aim is to give an overview of aptamers, highlight the opportunities of their application as means of effective therapeutic tools as well as functionalize them as potential diagnostic probes. Furthermore, the diverse modifications of aptamers for theranostic purposes, including therapeutic agents and targeted delivery nanomaterials, are comprehensively summarized.

Keywords: Aptamers, Bionanomaterials, Nanomaterials, Theranostics.

INTRODUCTION

Over the last decade, theranostic bionanomaterials have emerged as an invaluable tool in personalized medicine [1]. The term theranostics refers to the combination of molecular imaging and therapy. Indeed, some bionanomaterials per se have

* **Corresponding author Walhan Alshaer:** Cell Therapy Center The University of Jordan Amman 11942, Jordan; Tel: (+962) 790823678; E-mail: walhan.alshaer@ju.edu.jo

very interesting therapeutic and diagnostic characteristics [2]. Recent progress in nanomaterials technology and aptamer-based targeting molecules have provoked efficient theranostics models.

Aptamers are functional single-stranded DNA or RNA oligonucleotides ranging in size from 5 to 30 KDa that can fold into unique three-dimensional structures, providing an ability to bind their targets with high affinity and selectivity [3, 4]. Aptamers were first described in 1990 by two independent groups. Tuerk and Gold worked on translational regulation of the DNA polymerase gene to find nucleic acid ligands that interact with T4 DNA polymerase and repress its activity in an attempt to get a better understanding of the recognition site. By the end of their experiment, they were able to produce a high-affinity RNA ligand through a novel protocol termed SELEX (Systematic Evolution of Ligands by EXponential enrichment). In the meantime, Ellington and Szostak isolated specific RNA ligands capable of binding organic dyes, and they, in turn, called these ligands as Aptamers [5, 6]. Since the discovery of aptamers, several major advances have been witnessed in the aptamers field. A main progress was achieved by introducing chemical modifications of aptamers, thereby enhancing stability and binding properties [7]. Moreover, aptamers were selected for a wide range of targets, including ions, small chemical molecules, peptides, proteins, infected cells, pathogens, and even cancer cells. In the following years, aptamers found their way into several applications involving diagnostics, therapeutics, regulation of gene expression, high throughput screening, and targeted drug delivery. In 2004, Macugen® (pegaptanib sodium) was announced as the first aptamer FDA approved for the treatment of age macular degeneration disease (AMD).

Theranostics bionanomaterials have been created great growth avenues for the development of precision medicine. Various aptamer-dependent systems were successfully developed for molecular imaging and targeted therapy. The focus of the current chapter is to highlight the utilization of aptamers as targeting molecules for theranostic biomaterials. Aptamers are increasingly proving to be a powerful tool in research and drug development for various conditions, with minimal effect on healthy tissues by assuring more selective drug targeting and delivery and, thus, better therapeutic efficacy and potency.

APTAMERS

The word Aptamer is derived from the Latin “aptus”, which means “fit” and the suffix “-meros” which means “portion”. An Aptamer is a single-stranded DNA or RNA molecule [4] obtained through Systematic Evolution of Ligands by EXponential enrichment (SELEX). An Aptamer’s binding to its target is quite specific. Aptamers are also known as chemical antibodies, like antibodies; they

bind to targets with high affinity, modulate target function, deliver cargo to specific sites, and are used in diagnostic and analytical assays, whether in solution or immobilized forms. However, aptamers surpass their proteinaceous counterparts by their low immunogenicity, physical stability, facile chemical modification, and the relative ease of their large-scale synthesis at affordable costs with little or no batch-to-batch variation. These alluring properties have propelled aptamers to the forefront of therapeutic and diagnostic agent development as well as bio-sensing platform construction [3]. Numerous aptamers have been developed during the past 2 to 3 decades for a variety of medical applications, such as chemical sensors, imaging molecules, diagnostic assays, and active therapeutic molecules [4].

Aptamers can be generated using either DNA or RNA oligonucleotides. Both types act similarly as binding molecules. However, RNA aptamers are widely believed to produce more complex 3D structures, whereas DNA aptamers are more stable and have a lower cost of production [8]. Although several unmodified DNA and RNA aptamers have been successfully selected for different targets, these aptamers are highly susceptible to degradation by nucleases and rapid clearance from the circulation. Therefore, several chemical modifications have been applied and investigated at different parts of the aptamers sequences. These chemical modifications were shown to improve the physio-chemical properties of the aptamers, increasing their stability, bioavailability, diversity, and establishing hydrophobic interactions [3, 9].

The backbone (phosphate/ribose) of the aptamer sequence is a common site for chemical modification. A common modification is the introduction of the phosphorothiolated linkage instead of the normal phosphodiester linkage. However, thiolated aptamers may induce toxicity and nonspecific interactions. When it comes to RNA aptamers, ribose sugar is the preferred site for modifications. The ribonuclease A (RNase A) targets 2'-hydroxyl group of ribopyrimidines and breaks the phosphodiester bond in the sugar-phosphate backbone of RNA strands. Thus, substituting the 2'-hydroxyl group of ribopyrimidines by 2'-amino, 2'-fluoro, or 2'-O-methoxy groups lead to a significant increase in the stability of RNA. Several reports showed that the 2'-amino modification increases the RNA half-life in serum to 170 hours compared to 10 seconds of the unmodified RNA aptamers. However, the 2'-amino modification affect thermodynamic stability of the aptamer, thus hindering binding affinity [10]. On the other hand, 2'-fluoro modifications also increase stability with half-life around 90 hours in serum. This type of modification was used in Macugen® development [11]. Moreover, 2'-fluoro modifications showed better base pair stability and binding affinity of the aptamers [11]. Another interesting approach to develop nuclease-resistant and stable aptamers is through

CHAPTER 7

Viral and Non-viral Nanoparticles for Gene Therapeutics

Hassan Elsana¹ and Amal Ali Elkordy^{*,1}

¹ School of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences and Wellbeing, University of Sunderland, Sunderland SR1 3SD, UK

Abstract: The recent accomplishment of the human genome and DNA discovery has led to the diagnosis of many diseases caused by imperfections in genes. These diseases involve gross disturbances in the number or arrangement of a person's chromosomes. Hence, gene therapy has become a promising new therapy for the treatment of somatic diseases, for example, malignant tumours [1], severe infectious diseases, such as AIDS [2], and many genetic disorders, including haemophilia and cystic fibrosis [3]. Gene therapy introduces a gene into human cells to replace, delete, or correct gene function to produce a therapeutic protein with the desired action. This adjustable gene can be used to cure any disease. In 1990, a gene therapy clinic was initiated to find treatment for severe combined immunodeficiency (SCID). However, the first success of gene therapy was not observed until 2000 when Cavazzana calvo *et al.* [4] reported a success using gene therapy for the treatment of SCID [4]. While it has been 30 years since the first gene therapy trial, gene therapy is still a high-risk treatment, and only a few drugs have been approved, such as Glybera[®], Gendicine[®], and Strimvelis[®].

Keywords: Dendrimers, Gene therapy, Liposomes, Non-viral vectors, Viral vectors.

INTERNAL AND EXTERNAL BARRIERS TO GENE THERAPY

The delivery of genes into eukaryotic cells faces many barriers. It is estimated that the half-life of naked DNA is ten minutes following intravenous injection [5]. Many nucleases present in the extracellular matrix will rapidly degrade unprotected nucleic acid following systemic administration. Phagocytes, such as Kupffer cells in the liver, and resident macrophages in the spleen, are responsible for the clearance of DNA-loaded colloidal particles administered through blood circulation. In addition, poor penetration due to high hydrophilicity, hepatic first-

* Corresponding author Amal Ali Elkordy: School of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences and Wellbeing, University of Sunderland, Sunderland SR1 3SD, UK; E-mail: amal.elkordy@sunderland.ac.uk

pass metabolism, and a highly negatively charged phosphate backbone of DNA prevent its passage across negatively charged cellular membranes.

For this reason, the encapsulation of plasmid DNA in order to protect it and increase circulation time is a crucial step in developing gene therapy. In addition, the mechanism of gene therapy release from endosomes and lysosomes can significantly impact gene degradation in lysosomes; Fig. (1) shows a chart for the gene delivery pathway, an illustration of the gene pathway, and barriers to its delivery [6]. Macromolecules captured within the endosomes usually transform into digestive lysosomes unless some escape mechanisms are used to intercept this maturation process.

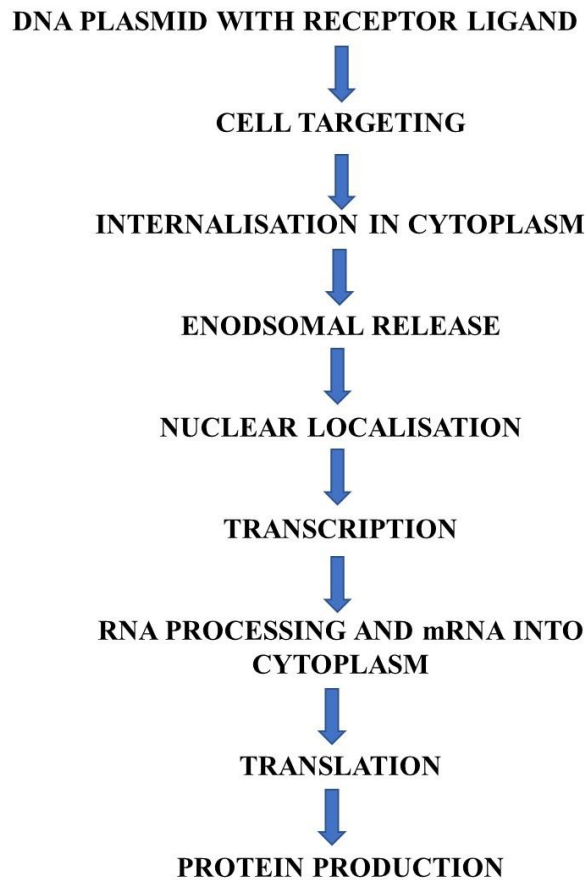


Fig. (1). A chart for the gene delivery pathway.

GENE DELIVERY METHODS

The gene delivery system is an initial phase in the achievement of gene therapy. Polynucleotide molecules (*e.g.*, plasmid DNA, RNA, and antisense oligonucleotides) are sensitive and hydrophilic, with a negatively charged phosphate backbone at physiological pH. Such physicochemical properties restrict their binding to and passive diffusion across lipophilic cell membranes. Moreover, they are rapidly degraded in biological fluids and do not accumulate in target tissues following systemic administration. In order to successfully transfect DNA into cells, DNA must be condensed and protected against nuclease degradation.

Additionally, the negative charge of DNA must be masked in order to allow entry through the negatively charged cell surface. After loading the genetic material to the vector, the vector must be delivered to the blood vessels and must be stable enough to avoid clearance by albumin due to their high surface charge. Next, the vector must pass through the epithelial tissues of the blood vessels and enter the target cell through the endocytosis process [7, 8]. Fig. (2) shows the most commonly used non-viral vectors in gene therapy.

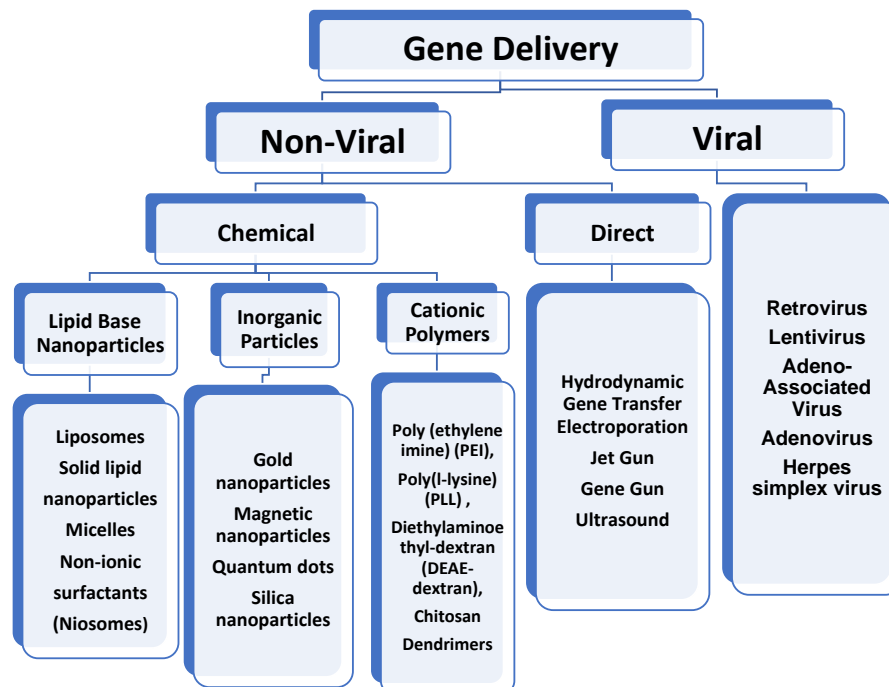


Fig. (2). The most commonly used non-viral vectors in gene therapy.

CHAPTER 8

Conclusion, Outlook, and Prospects: Bionanomaterials in Clinical Utilization

Alaa A A Aljabali^{1,*}, Kaushik Pal², Rasha M. Bashatwah¹ and Murtaza M. Tambuwala^{3,*}

¹ Faculty of Pharmacy, Department of Pharmaceutics and Pharmaceutical Technology, Yarmouk University, Shafiq Irshidat Street, Irbid 21163 - P. O. BOX566, Jordan

² University Centre for Research and Development (UCRD), Department of Physics, Chandigarh University, Mohali, Gharuan, Punjab 140413, India

³ SAAD Centre for Pharmacy and Diabetes, School of Pharmacy and Pharmaceutical Science Ulster University, Coleraine, UK

Abstract: Nanomaterials have contributed to significant advancements in the realms of biotechnology and medicine. A holistic examination of the different biocompatible nanocomposites is discussed in this chapter. Their compatibility with state-of-the-art engineering techniques, such as additive manufacturing to design practical surgical implants, is also discussed. The importance and potential of nanocomposites and manufacturing processes in implantable medical device industries are also thoroughly considered. Nanomaterials' unique characteristics contrast with their large counterparts, such as high surfaces, reactivity, and reproducibility. Their incorporation in matrices has shown that the resultant composites' mechanical, chemical, and physical properties can be improved.

Consequently, a wide variety of technical technologies, such as energy products, biomedical applications, micro-electrical equipment *etc.*, have been intensively researched. Furthermore, the foundation for many new medicines and surgical instruments, including nanorobots, has been built on nanobiotechnology. It has been utilized in almost every medical sector, and its usage in the treatment of different diseases, such as cancer, neurobiology, cardiovascular disorders, joint and bone disorders, eye diseases, and infectious diseases, has been evident through different studies. Nanobiotechnology can promote diagnostics and the advancement of customized medicine, *i.e.*, prescribing unique therapeutics that are tailored to an individual's needs. Many advances have already begun, and a definite effect on medicine practice will be felt in a decade.

* Corresponding authors Alaa A A Aljabali and Murtaza M. Tambuwala: Faculty of Pharmacy, Department of Pharmaceutics and Pharmaceutical Technology, Yarmouk University, Shafiq Irshidat Street, Irbid 21163 - P. O. BOX 566, Jordan and SAAD Centre for Pharmacy and Diabetes, School of Pharmacy and Pharmaceutical Science Ulster University, Coleraine, UK; E-mails: alaaaj@yu.edu.jo and m.tambuwala@ulster.ac.uk

Keywords: Naturally occurring nanoparticles, green synthesis, nanomaterials, bacteriophages, biodegradation, biosynthesis.

INTRODUCTION

In recent years, nanotechnology and nanobiology have gained a significant boost. The latest growth in the applications of polymer composites is gathering momentum worldwide. Biotechnology has been revolutionized as an assertive discipline utilizing bionanotechnological research and development. Surface functionalization at nano-levels is a crucial aspect of bionanotechnology, in which several entities have already been exploited. Bio-nano substances can be used for diagnostic and therapeutic purposes by using polymers, bacteria, nucleic acids, antibodies, or other proteins [1]. Bionanotechnological advancement has made early diagnosis and treatment more possible. This makes perfect sense since more lifetimes will be spared if doctors can promptly diagnose lethal disorders and diseases. Bionanotechnology is referred to as an inspirational catalyst in a nanotechnology discipline. Speculation is being made that progress will be made more and more as biotechnology integrates [2, 3].

The extraordinary features and establishment of advanced polymer composites with established environmental analytical techniques contribute to the tremendous success of boosting the environment research era. Over the last few decades, nanotechnology's development has been fueled by the need for new nanomaterials with unmatched properties from their counterpart synthetic nanoparticles. Such properties include biodegradability, biocompatibility, and unmatched uniformity in structure and composition, with the amenability of chemical and biological modification to impart new and novel properties that make biomaterials ideal nanoparticles [4]. Newly developed nanomaterials showed promising medical, pharmaceutical, environmental, and energy applications. This chapter highlights different types of nature-inspired and biosynthesized nanomaterials and their green synthesis methods and some of their emerging applications, especially in nanomedicine, cosmetics, drug delivery, molecular imaging, and catalytic precursors. The chapter covers different types of bionanomaterials (*e.g.*, viruses, protein cages, phages) and highlights their unique properties and potential applications [5, 6].

Treating certain illnesses is a big challenge in delivering treatment compounds to the target site. A typical drug application may be constrained in potency, poor biodistribution, and lack of selectivity. Nanocages have been shown to be preferentially clustered in tumors or inflammatory sites due to antigen sampling due to the improved vasculature permeability and retention (EPR) effect. Present means of treating the bulk of solid tumors are surgery and chemotherapy or

radiation treatment. However, today's therapy destroys healthy tissue and induces unjustified patient toxicity in its general and systematic implementation. Nanoparticulate delivery systems in various biomedical applications have been used in recent times. The attributes of these products are biocompatible, well-defined, and readily functional materials. Mainly due to these materials' properties, nanomaterials demonstrate high differentials in the cell or tissue-specific targeting and absorption ability. Besides, before hitting the target, the drug molecule on the nanocarrier is shielded from harsh conditions. Contrary to standard drug delivery, a delayed and regulated release of drugs can be accomplished with nanomaterials. Therefore, nanomedicine represents a revolutionary field of tremendous treatment potential by combining intelligent nanoparticles with a wide variety of functions [7].

ADVANTAGES OF NANOBIO TECHNOLOGY

The pathophysiology and the anatomic modifications of diseased or inflamed tissue have paved various ways for producing targeted nanotechnology products. In the following respects, this growth is advantageous: 1. The pathophysiological properties of diseased tissues may be used to target drugs; 2. Different nanoproducts can accumulate at concentrations above standard medicinal products; 3. Enhanced vascular permeability in tumors and impaired lymph drainage enhance tumors or inflamed tissue effects of nanosystems by improved dissemination and retention. 4. The potential of the nanosystems to locate inflammatory tissues is selective. 5. Nanoparticles may be used to supply/transport medicines to the brain that overcome the blood and brain barrier (meninges). 6. Nanoparticle loading modifies the distribution of cells and tissues and contributes to the targeted delivery of biologically active substances to increase drug production and mitigate drug toxicity [8, 9].

Applications of Nanobiotechnology in the Biomedical Field

Several therapeutic uses of nanobiotechnology are currently being studied on various topics, such as cancer detection, target drug delivery, and molecular imaging. Clinical trials are now underway on several new, exciting drugs. These innovative applications of biological systems will undoubtedly be the basis for future diagnosis, care, and disease prevention. The optimum utilization over alteration and functionalization of certain noncarrier is a significant and critical aspect to be taken into consideration when NPs are used as drug delivery system; two fundamental principles, surface alteration and targeting, are discussed here; these two concepts, nevertheless, can in some cases be used to the same degree. Altering processes are implemented for targeting purposes, including the defense

SUBJECT INDEX

A

- Absorption pathway 22
 Accumulation, tau protein 114
 Acid(s) 6, 9, 20, 22, 38, 39, 52, 53, 67, 87, 88, 89, 90, 91, 100, 114, 137, 150, 151, 168, 169, 170, 178, 180, 181
 amino 180
 carboxylic 100
 chloroauric 169
 cholic 150
 etching 137
 folic 22
 folinic 67
 glycolic 91
 Hyaluronic 88
 lactic 91
 lactic-co-glycolic 52, 91
 nucleic 22, 38, 39, 87, 88, 89, 90, 168, 178, 180, 181
 oleic 20, 100, 114, 137, 170
 polyglycolic 6
 polylactic 6, 9
 Acquired resistance mechanisms 143
 Actin cytoskeleton 15
 Action, mitochondrial dehydrogenase 14
 Activation, microglial 114
 Activity 13, 16, 18, 60, 105, 114, 131, 135, 166
 antitumour 60
 bactericidal 18
 cationic lipid transfection 166
 intrinsic enzymatic 105
 microglial 114
 mitochondrial dehydrogenase 16
 Acute 61, 63, 66
 lymphoblastic leukaemia 63
 myeloid leukaemia (AML) 61, 63, 66
 Additional technological development 59
 Adeno-associated viruses 162
 Adenoviruses 34, 162
 replicating 34
 Adenovirus vector 163
 Adhesion and cellular behavior 5
 Adipose derived stem cells (ADSCs) 111
 Advantages of nanobiotechnology 179, 188
 Agents 1, 5, 10, 31, 35, 58, 66, 84, 88, 135, 136, 137, 142, 143, 145, 147, 181, 183, 184,
 amphiphilic polymeric stabilising 58
 anticoagulant 10
 anti-infective 135
 antimicrobial 1
 anti-thrombotic 136
 biodegradable 5
 bio-imaging 143
 hydrophobic chemotherapy 142
 immunotherapeutic 31
 nano-theranostic 137
 photosensitizing 143
 photothermal 147
 safe anticancer 147
 semi-synthetic chemotherapeutic 66
 sensitizer 145
 susceptible 184
 theranostic 84, 88
 viral infectious 135
 Aggregates 24, 104, 166
 amyloid 104
 AgNPs, amine-functionalized 18
 AIDS-related Kaposi's sarcoma 64
 Alzheimer's disease 113
 Amphiphilic 165
 Amphotericin 64, 68
 Anthracyclines 136, 147
 Antibiotics 10, 86
 antitumor 86
 Antibodies 16, 33, 51, 52, 91, 104, 105, 130, 131, 151, 178, 182, 183
 encapsulated secondary 105
 monoclonal 16, 104, 130
 Anticancer 71, 113
 agents salinomycin 113
 therapeutics 71
 Anticancer drugs 58, 86, 115, 117, 139, 148
 conventional 115
 water-soluble 58

- Antigens 32, 35, 36, 40, 52, 89, 117
tumor 117
- Antioxidant cell pathway 20
- Apoptosis 15, 114, 115, 117, 143, 145, 147
induced cell 115
inducing 147
- Apoptosis pathway 115
- Application(s) 2, 3, 4, 5, 6, 10, 11, 12, 13, 30,
31, 68, 69, 70, 99, 101, 102, 105, 106,
109, 110, 111, 112, 113, 114, 118, 151,
177, 178, 179, 184
- bioimaging 10
- biomedical 2, 99, 102, 118, 177, 179
- chemotherapeutic 112
- diverse 11
- emerging 178
- immunotherapeutic 30
- industrial 13
- medicinal 2
- of MNPs in neurodegenerative diseases 113
- of nanobiotechnology 179
- surgical 3
- theranostic 69
- therapeutic 6
- translational 101, 151
- Aptamers 131, 132, 133, 135, 142, 144, 145
anti-nucleolin 135, 142, 144
fluorescent-labeled 145
immobilized 135
sensing 135
thiolated 132
utilization of 131, 133
- Asymptomatic chronic lymphocytic 63
leukaemia 63
- Atherosclerosis 103
- Autoimmune diseases 51, 114
- Autoradiography 16
- B**
- Bacterial adhesion 4
- Bilayer 54, 170
- fluidity 54
nanoparticle-supported lipid 170
- Binding 52, 131, 135, 166
ligand-receptor 52
properties 131
serum proteins 166
thrombin 135
- Biodegradability 9, 53, 102, 178
- Biodegradable nanomaterials 23
- Bioimaging agent delivery 69
- Biomarkers 49, 51, 71, 186, 190
- Biomaterials 1, 2, 3, 4, 5, 6, 7, 9, 11, 13, 14,
15, 16, 17, 21, 24, 131
applications of 6, 7
cytotoxicity of 15, 17
degradation 24
destructive 7
harmful 13
hydrophobic 15
metal 5
polymer-based 3
theranostic 131
- Biosensors 2, 105, 134, 151, 186, 190
aptamer-based 151
glucose 105
prognostic 105
- BLA application 87
- Blood 3, 4, 12, 21, 37, 67, 68, 104, 113, 114,
115, 188, 190
adhesions 3
brain barrier (BBB) 12, 37, 68, 104, 113,
114, 188, 190
capillary occlusion 21
coagulation 4
pressure 67
-spinal fluid barrier 115
- Bone 4, 5, 7, 8, 9, 50, 177
arthritic 8
disorders 177
erosion 5
marrow transplants 7
regeneration 4

Subject Index

Breast cancer, metastatic 61, 64, 67, 186
Bunionectomy 65
Burkitt's lymphoma cell 144

C

Calcium phosphate ceramics 6
Cancer 31, 33, 34, 40, 41, 49, 50, 51, 52, 64, 84, 85, 86, 87, 88, 98, 151
 bladder 34
 cervical 64
 colon 86
 immunotherapy 30, 31, 34, 35, 37, 40, 41, 53, 62, 63, 64, 67, 117, 116, 84, 85, 86, 91, 92, 115, 116, 145, 148, 186
 liver 34
 metastatic 30
 ovarian 62, 64, 67, 186
 stem cell (CSCs) 116
 therapy 34, 37, 84, 85, 91, 92, 115, 116, 145, 148
 urothelial 62
 uterine 35
 vaccines 30, 37, 40
Carcinogenesis 50, 143
Carcinogenicity 9
Carcinoma, renal cell 187
Cardiotoxicity 60, 61
 doxorubicin-related 60
Cardiovascular diseases 98, 103, 115, 135
Cationic 89, 165, 166
 amino acids 89
 lipid release 166
 lipids and cationic polymers 165
 polysaccharide 89
Cationic polymers 87, 89, 91, 161, 165, 167, 168
 synthetic 89
Cell 4, 13, 14, 15, 16, 19, 143
 adhesion 4, 15
 culture in polystyrene tissue 16
 death 13, 14, 16, 19, 143

Bionanotechnology: Next-generation Therapeutic Tools 197

 lysis 14
 monolayers 15
 protein 16
Cellular enzyme 13
Cellulose 5, 139, 149
 polyvalent carboxymethyl 139, 149
CEM 139
 cancer cell killing 139
 tumors 139
Central nervous system (CNS) 12, 50, 68, 190
Cerebral edema 39
Cerebrospinal fluid 12
Chemical 5, 16, 37, 130, 131, 132, 151, 165
 based vectors 165
 modifications 5, 37, 130, 131, 132, 151
 processes 16
Chemotherapeutic agents 85
Chitosan 9, 20, 53, 89, 104, 161, 169
 cationic polysaccharide 169
Chromosomes, person's 159
Chronic myeloid leukaemia (CML) 63
CNS toxicity 1
Combination 35, 57
 lipids-drug 57
 treatments 35
Computed tomography 102
Computer image analysis 16
Computerised tomography (CT) 69, 102, 141, 149, 151
Contrast agents 69, 102, 103, 107
 biocompatible MRI 107
 conventional paramagnetic MRI 103
Corrosion 4, 5, 100
 protection 4
 resistance 5
Corrosive nature 4
COVID-19 pandemic 105
Covid-19 vaccines 87, 92
Cryopreservation 110
Cysteamine 105
Cystic fibrosis 159
Cytarabine 66, 67

- delivering 66
- Cytocompatibility 11
- Cytokines 13, 39
 - pro-inflammatory 39
- Cytoplasm 18, 104, 143, 162, 167
- Cytoplasmic release 15
- Cytotoxicity 1, 11, 13, 14, 15, 16, 17, 18, 20, 70, 139
 - nanomaterial 18
 - tests 14
- D**
- Damage 14, 18, 19, 20, 85, 103, 107, 112, 113, 114, 145
 - genotoxic chemicals cause gene 14
 - nerve 107
 - nuclear 19
 - oxidative retinal 112
 - reduced cellular 20
 - synaptic plasticity 113
- Deficient anemia 187
- Degeneration 8, 22, 65, 113, 135
 - age-related macular 65, 135
 - chronic progressive 113
 - knee 8
- Degenerative disease 168
- Degradation 22, 24, 68, 115, 132, 151, 161, 162, 165, 168, 169, 184
 - enzymatic 22, 165
 - lysosomal 162
 - non-enzymatic 22
 - nuclease 115, 161
- Delivery 2, 62, 84, 85
 - of chemotherapeutics 85
 - programs 2
 - vehicles 62, 84
- Delivery systems 60, 70, 111, 162, 165, 172, 187
 - developed drug 187
 - germline gene 162
 - lipid nanoparticles drug 70
 - non-viral chemical-based gene 165
 - nonviral gene 172
 - somatic gene 162
- Dendritic cell(s) (DCs) 35, 38, 117
 - immunotherapy 117
- DepofoamTM technology 65
- Deposition 86, 101, 102
 - chemical vapor 101
- Derivatives 23, 58
 - cyclodextrin 23
- Detection 49, 51, 56, 71, 103, 104, 105, 106, 134, 135, 136
 - atherosclerotic plaque 103, 104
 - based assays 105
 - real time RT-PCR 106
 - sensitive 106
- Development, nanotechnology's 178
- Devices 2, 8, 10, 56, 87, 159, 172, 177
 - cardiac 2
 - polymeric 10
- Diabetic retinopathy 112
- Diagnosis, bio-sensing 99
- Differentiation, osteogenic 110
- Disorders 106, 181
 - cardiovascular 177
 - genetic 87, 159, 172
- Display magnetic properties 102
- DNA 11, 14, 15, 16, 50, 86, 112, 114, 131, 132, 133, 136, 145, 159, 161, 162, 163, 164, 165, 166, 167, 168, 169, 181, 185, 186
 - anticancer 145
 - cellular 16
 - chromosomal 163
 - condense 165
 - damage 11, 14, 86, 100
 - delivery 114, 169
 - detection methods 186
 - double-stranded 162
 - for gene delivery 162
 - fragmentation 15
 - naked 159, 164

- polyethylenimine-plasmide 112
 - polymerase gene 131
 - reducing nuclear 15
 - related apoptosis 15
 - repair genes 50
 - sequencing tests 15
 - synthesis 16
 - transfer 165
 - viruses 162
 - DNA aptamers 132, 134, 135, 148
 - anti-adenosine 134
 - DNA-based 162, 164
 - treatment 164
 - viral vectors 162
 - Double emulsion method 58
 - Drug(s) 31, 41, 56, 65, 69, 185
 - immunotherapeutic 31, 41
 - injectable 185
 - lipophilic 69
 - loading capacity 56
 - therapeutic 65
 - thermosensitive 58, 59
 - Drug delivery 9, 12, 19, 49, 51, 53, 54, 67, 90, 98, 99, 111, 112, 114, 115, 131, 139, 148, 170, 179, 185, 186
 - device 9
 - efficacy 19
 - liposomal 67
 - magnetic 170
 - methods 9
 - pathway 12
 - small-molecule 90
 - systems 9, 148, 179
 - targeted 131, 139
 - Drug release 68, 139
 - in situ 139
- E**
- Effects 10, 16, 18, 57, 63, 87, 114, 116, 145
 - cytotoxic 16, 116
 - immunogenic 114
 - oligodynamic 18
 - photothermal 145
 - proton-sponge 87
 - synergistic 10, 57, 63
 - Efficacy 15, 35, 37, 39, 51, 64, 131, 136
 - therapeutic 131, 136
 - Egg phosphatidyl glycerol (EPG) 65
 - Electroporation 164
 - Embryonic 106, 107, 110
 - cardiac cells (ECCs) 110
 - stem cells (ESCs) 106, 107
 - Emulsifiers 24
 - Emulsion preparations 57
 - Encoded DNA polymerases 162
 - Endocytosis 18, 19, 138, 161, 162
 - caveolae-mediated HDF 19
 - process 161
 - Endonucleases 15, 151
 - Endothelial cells 22, 23, 113, 115, 171
 - glomerular 23
 - transfected vascular 115
 - vascular 115
 - Endothelial monolayers 142
 - Enhanced permeation and retention (EPR) 21, 52, 102, 171, 178
 - Epidermis 21
 - Epoxide hydrolase 22
 - Escape 87, 91, 92, 162, 165, 167, 169
 - endosomal 87, 92, 162, 165
 - endosome 91
 - European medicines agency (EMA) 64, 66, 116
 - Exonucleases 151
 - Expression 35, 63, 66, 88, 103, 162, 163, 164
 - abnormal 35
 - Extracellular vesicles (EVs) 40, 108
 - Extraction 19, 106
 - high quality RNA 106
 - Eye diseases 177
- F**

- Fatal 12, 50
 bradyarrhythmia 12
 diseases 50
Fatty acids 6, 55, 57, 68, 166, 170
 long-chain 57
Fibroblasts 14, 17, 18, 19
 dermal 19
Fluorescence 104, 134, 138, 141, 143, 147,
 149, 150, 151, 170, 182
 conjugated magnetic 143
 imaging techniques 104
 property 141
 tumor 147
Fluorescent 141, 142, 150, 170, 181
 dye 141, 142, 150, 181
 nanocrystals 170
Food 34, 53, 64, 66, 67, 68, 90, 105
 and drug administration (FDA) 34, 53, 64,
 66, 67, 68, 90
 pollutants 105
Foot syndrome 60
Formulation 60, 62, 70, 112, 116, 167
 designing lipid-based nanoparticles 70
 lipid-based 60
 nanomagnetosome inhalation 112
 nanoparticle thermal therapy 116
 niosome 167
 novel polymeric micellar 62
 novel sustained-release micellar 62
Functional 31, 34, 130
 genes 31, 34
 genomics 130
Functions 13, 18, 58, 67, 135, 136, 143, 179,
 181, 188
 cellular 18
 damaged organ 188
 inhibiting miRNA 143
 metabolic 13
 renal 67
 therapeutic 136
Fusion, lymphocyte 13
- G**
- Gelatin polypeptide 90
Gemcitabine 62
Gene(s) 30, 31, 37, 50, 62, 66, 84, 87, 104,
 114, 115, 131, 159, 160, 161, 162, 164,
 166, 169, 170, 184
 damaged 184
 delivery system 161
 encoding 37
 expression 104, 131, 170
 pathway 160
 stability 115
 suppressor 62
 therapeutic 30, 164
 transfer 166
 tumour suppressor 50
Gene delivery 160, 161
 methods 161
 pathway 160
Gene therapy 30, 37, 60, 111, 114, 159, 160,
 161, 163, 165, 167, 172, 184
 programs 184
 release 160
Genetic treatment 2, 10
Genotoxicity 13, 14, 17
Glassy carbon electrode (GCE) 105
Glioblastoma 37, 64, 142
 therapy 142
Glomerular 22
 capillaries 22
 filtration 22
Glucose oxidase 105
Glycoproteins 65, 66
 fusion-active 65
 influenza surface 66
Glycyrrhetic acid and galactose 22
Granulomatous inflammation 13
Green 104, 170, 178
 fluorescent protein (GFP) 104, 170
 synthesis methods 178

Subject Index

Growth 3, 7, 16, 24, 50, 116, 117, 178, 179, 184
 impaired biomaterial 24
Growth factors 10, 63, 112, 135, 171, 109
 epidermal 171
 vascular endothelial 112, 135

H

Hazardous 10, 11, 13, 14, 19
 chemicals 14
 substance 13
Heat energy 145
Hemagglutinin 66
Hemolysis 14
Heparin 10
Hepatitis 39, 65, 187
 A vaccine (HAV) 65, 187
Hepatocellular carcinoma 63, 103
Hepatocytes 22, 23, 89, 104
Hepatotoxicity 10, 34, 70
Hereditary transthyretin amyloidosis 68
Herpes simplex virus 162, 164
High-pressure homogenization (HPH) 56
HIV 113, 135, 186
 associated Kaposi's sarcoma 186
 infection 113, 135
Human foamy virus (HFV) 162
Hybridization chain reaction (HCR) 136
Hydrolysis 6, 9, 91, 180
 alkaline 180
Hydrophilic 18, 20, 54, 84, 89, 100, 161, 167
 carbohydrate 54
 hydrophobic coating 20
Hydrophilicity 3
Hydrophilic 53, 58
 lipophilic balance (HLB) 58
 properties 53
Hydrophobic drugs 69, 86, 88, 167
Hydrophobicity 3, 92
Hyperthermia 61, 99, 116
 -based treatment applications 99

Bionanotechnology: Next-generation Therapeutic Tools 201

microwave 61

I

Illnesses, neurological 113
Imaging 141, 142, 186, 190
 applications 186
 genetic 190
 glioma 142
 system 141
Immune responses 31, 33, 35, 37, 39, 40, 70
 systemic 35
 targeted 37
Immune system 31, 33, 34, 35, 36, 40, 50, 53, 180, 181, 184
Immunity 33, 36, 37, 184
 adaptive 33
 innate 37
 systemic 36
Immunodeficiency 163
Immunofluorescence microscopy 15
Immunotherapy 30, 31, 32, 33, 34, 35, 37, 38, 39, 40, 41, 51, 84
 effective cancer 30
 viral 34
 virus-based 41
Industry 54, 57, 184, 187
 cosmetic 54
 medical 184
Infection 1, 5, 31, 37, 98, 114, 134, 182, 183
 bacterial 5
 coronavirus 31
 pathogen 98
 pathogenic 134
 viral 114
Infectious diseases 31, 38, 41, 87, 135, 177
Inflammation 5, 11, 17, 52, 188, 189
 interstitial 189
 peribranchial 189
Inflammatory 63, 190
 bowel diseases 190
 diseases 63

reactions 190
 Influenza vaccine 187
 Infrared heptamethine 150
 Inhibition, targeted 151
 Injuries, induced myocardial 110
 Interactions 18, 20, 91, 147, 167, 181
 hydrophobic 167
 leached ion 18
 ligand 20
 ligand-receptor 91
 protein-protein 147
 protein-RNA 181
 Intracellular trafficking 168
 Intracranial glioma 39
 Iron 11, 107, 187
 carboxymaltose 187
 deficiency 107
 homeostasis 11

K

Kaposi's sarcoma 68, 186
 Kupffer cells 103, 159

L

Lactate dehydrogenase 14
 Lateral flow assay (LFA) 105
 Leukemia, acute myeloid 66, 67
 Lipid(s) 50, 52, 53, 54, 55, 56, 57, 69, 70, 87,
 165, 166
 biocompatible 55
 chelator-conjugated synthetic 69
 -drug conjugates (LDCs) 55
 nanoparticles 50
 -nanoparticles toxicity 70
 Liposomal amphotericin 186
 Liver 11, 70, 186, 187
 enzymes 70
 function 11
 Kupffer cells 11
 lesions 186

neoplasms 187
 Lung 18, 189
 fibroblasts 18
 necrosis 189
 Lymphocytes 33
 Lymphoma 50, 51
 Lysosomes 22, 144, 160, 162, 168

M

Macrophages 1, 12, 13, 20, 23, 33, 64, 103
 alveolar 13
 pulmonary 1
 Maemorrhoidectomy 65
 Magnetic 68, 69, 84, 98, 102, 104, 107, 108,
 113, 137, 138, 143, 145, 149, 151
 field enhanced convective diffusion
 (MFECD) 113
 fluorescence (MF) 143
 hyperthermia treatment 116
 resonance imaging (MRI) 68, 69, 84, 98,
 102, 104, 107, 108, 137, 138, 145, 149,
 151
 Measure cell adhesion 15
 Medical imaging 68, 69
 Medications 71, 180, 182
 anticancer 180
 lipid-based nanomaterial 71
 Medicinal polymers 2, 9
 purposely humiliating 9
 Mesenchymal stem cells (MSCs) 106, 107,
 108, 109, 110
 Mesoporous silica nanoparticles (MSNs) 170,
 171
 Metabolite transport mechanisms 13
 Metalloprotein 24
 Metastases 31, 49, 50, 51, 71, 104, 187
 imaging lymph node 187
 Microscopy 15, 115, 182, 183
 confocal fluorescence 115
 electronic 182

Subject Index

Microtomography 109
Mononuclear phagocytic system (MPS) 21,
51, 54, 66
Monooxygenases 22
Morphology, icosahedron 181
Movement disorders 114
MRI contrast imaging agents 104
Mycobacterium tuberculosis 135
Myelodysplastic syndrome 63
Myeloma 50
Myocardial 12, 103, 187
 electrophysiology 12
 infarction 103, 187

N

Nanocarriers, therapeutic 88
Nanostructured lipid carriers (NLCs) 53, 55,
56, 68, 69
Nanosystems, theranostic 141
Nanotheranostic system 147
Necrosis, cellular 145
Nerve growth factor (NGF) 112, 113
Neuraminidase 66
Neurodegenerative diseases 99, 113
Neurological Disorders 113
Neuronal plasticity dysregulation 113
Neurotoxicity 172
Neutral redness 14
Neutrophils 33, 38
 tumour-infiltrating 38
Non-Hodgkin's lymphoma 67
Nucleases 132, 134, 159, 172
Nucleic acid drugs nanomaterials 142

O

Ocular 67, 99, 112
 diseases 99
 drug delivery 112
 histoplasmosis 67
Oil 57, 58, 86

Bionanotechnology: Next-generation Therapeutic Tools 203

 polyethoxylated castor 86
Oral mucosa fibroblasts (OMFs) 18
Orthopedic equipment 9
Osteosarcoma 67, 186

P

Palmar-plantar erythrodysesthesia 60
Parkinson disease (PD) 109, 113, 114
Phagocytosis 19, 101, 103
Photothermal therapy 144
Plasma integrity test 15
Plasmid DNA transportation 184
Polymeric nanoparticles, synthetic 32
Polymerization 10, 86
Polymers 2, 3, 5, 6, 7, 8, 9, 22, 53, 54, 55, 84,
87, 88, 89, 90, 92, 166
 amphiphilic 166
 non-immunogenic 84
 thermoplastic 7
Polymorphic cationic lipid 166
Polyneuropathy 67
Positron emission tomography (PET) 2, 69,
84, 88, 104
Progression 50, 67, 104
 prostate tumor 104
Progressive genetic alterations transform 50
Properties 3, 4, 5, 166
 additional biomaterial 3
 antimicrobial 5
 fusogenic 166
 osteointegration 4
Prostate cancer 40, 104, 105, 116
 diagnosis 105
Prostate-specific antigen (PSA) 105, 116
Proteins 2, 4, 10, 11, 13, 17, 21, 22, 37, 54,
87, 90, 104, 131, 133, 17, 178, 181, 182,
183
 adsorbed 4
 capsid 181
 chemotactic 13
 fluorescent 104, 183

green fluorescent 104, 170
immune-boosting 37
nasal 10
plasma 21, 54
Pulsed magnetic field (PMF) 107

R

Radiotherapy 33, 49, 60, 64
Rapid expansion of supercritical solution (RESS) 59
Reactive oxygen species (ROS) 11, 13, 17, 20, 116, 143, 144
Regenerative medicine 90, 106, 187
Reovirus-based oncolytic therapy 35
Reoviruses 35
Respiratory diseases 99
Retinal detachment 112
Reverse transcription 133
Ribonuclease 132
RNA 36, 39, 67, 86, 106, 114, 132, 133, 161, 162, 163, 165, 168, 169, 181
delivered short hairpin 114
dependent polymerase complexes 163
encapsulated 36
infectious 162

S

SELEX technology 133
Silica, mesoporous 110
Silica nanoparticles 147, 151
fluorescent 147
Silk fibroin (SF) 110
Single-photon emission computed tomography (SPECT) 88, 140, 151
Smart multifunctional nanostructure (SMNs) 137
Spontaneous emulsification method 57
Staphylococcal enterotoxin B (SEB) 105
Stem cells 51, 98, 106, 107, 108, 110, 111
membrane-derived mesenchymal 110

mesenchymal 106, 107, 108
transplanted 106
therapy 51, 98, 106, 108, 111
Stem cells human 106, 107, 108, 109, 110, 163
embryonic 107
induced pluripotent 110
mesenchymal 107, 108
Supercritical fluid extraction of emulsions (SFEE) 59
Superoxide dismutase 105
Superparamagnetic iron oxide nanoparticles 102, 106, 116, 170
Synovial joints 8
Synthetic 2, 3, 5, 7, 183, 91, 92, 100
chromophores 183
polymeric materials 2
polymers 3, 5, 7, 91, 92, 100
Systemic elimination of cationic lipids 166
Systems 12, 13, 24, 51, 61, 112, 113, 138, 141, 149, 169
mononuclear phagocyte 51
multimodal imaging 149
pulmonary 13
renal 12
respiratory 112
reticuloendothelial 24, 51, 113, 169
sensing 138, 141
thioredoxin-thioreductase 61

T

Target 142, 169
cancerous tissues 169
glioblastoma 142
Targeted drug transport (TDT) 136
Targeting prostate cancer 141
Technique
environmental analytical 178
magnetic separation 106

Subject Index

Theranostic 87, 88, 106, 130, 131, 133, 135,
136, 137, 139, 141, 143, 145, 147, 149,
151
 application of stem cells in regenerative
 medicine 106
 nanomaterials 130
 promising active targeting-based 148
Therapy 2, 34, 65, 66, 84, 87, 112, 114, 130,
135, 136, 138, 141, 142, 143, 144, 145,
179, 185
 diabetic retinopathy 112
 gemcitabine-based 66
 genetic 2
 neurodegenerative tauopathy 114
 photodynamic 65, 143, 144
 virus-based 34
Tissue(s) 2, 3, 4, 6, 7, 8, 9, 50, 89, 104, 107,
108, 111, 112, 166, 179, 188, 190
 damage 112
 disposition 107
 inflamed 166, 179
 inflammatory 179, 188
 repair 89
Tobacco 39, 50
 mosaic virus (TMV) 39
 smoke 50
Topoisomerases 86
Total hip replacement (THR) 8
Toxicity 1, 16, 62, 179, 188
 cisplatin-associated 62
 dermal 1
 engineered nanomaterials 188
 gastrointestinal 1
 influence 16
 mitigate drug 179
Transcytosis 21
Transfection pathway 166
Transferases 22
Triggering doxorubicin release 61
Triple-negative breast cancer (TNBC) 35

Bionanotechnology: Next-generation Therapeutic Tools 205

Tumor(s) 38, 39, 88, 90, 102, 103, 115, 117,
136, 137, 139, 142, 143, 149, 178, 179,
188
 metastatic 103



Alaa A A Aljabali

Dr. Aljabali is a nanoscientist by training with extensive experience in polymeric, metallic, lipid-based nanoparticles, and protein-based nanoparticles. Dr. Aljabali holds a Ph.D. from John Innes Centre in nanotechnology in the areas of viral nanoparticles. Dr. Aljabali worked as a Bionanotechnologist at JIC shortly after completing my Ph.D. and further 3 years as a postdoctoral fellow in cardiovascular medicine at Oxford University-UK. Dr. Aljabali has a proven track record in research with over 120 publications in top peer-reviewed journals in the primary research area of nanotechnology and its applications.

My lab's mission is to develop an innovative and novel frontier in biomaterials science and medicine through the design, development, and testing of novel natural bio-inspired materials using plant virus-based scaffolds, polymeric nanoparticles, and lipid-based nanomaterials. Leading a research laboratory interfacing bio-inspired, molecular engineering approaches with medical research, technology development, and materials science.



Kaushik Pal

Kaushik Pal received his Doctorate (PhD) in Physics from the University of Kalyani (India). Most recently awarded Honoris Causa Doctor of Science (D.Sc.) from Higher National Youth Skills Institute (IKTBN) Sepang, Govt. of Malaysia as well as achieved 'Gold Medal' awarded by the Prime Minister of Malaysia. Entire academic career Prof. Pal received the prestigious Marie Curie Postdoctoral Fellowship (Greece) offered by European Union Sponsorship, and the Chief-Scientist Faculty Fellow (PDF) nominated by Chinese Academy of Science (CAS) foundation in Wuhan University, China. As a distinguished academician, Prof. Kaushik has contributed innovative discoveries and smart teaching cultivated at the top-tier institutions and currently serving as an Associate Professor in University Centre for Research and Development (UCRD), Chandigarh University, Mohali. A well-known expert supervisor for PhD/Postdoctoral scholars and an experienced group leader to builds Inter- and cross multi-disciplinary Nanoscience excellence, resulted more than 125-significant articles in peer-reviewed (SCI/Scopus) International journals and partially edited or authored 26-renowned books with reputed publishers.