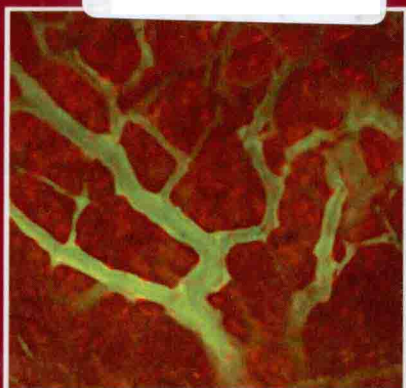


WOODHEAD PUBLISHING SERIES IN BIOMATERIALS



# **Biomaterials for cancer therapeutics**

Diagnosis, prevention  
and therapy

Edited by Kinam Park

**WP**  
WOODHEAD  
PUBLISHING



Woodhead Publishing Series in Biomaterials: Number 66

# Biomaterials for cancer therapeutics

## Diagnosis, prevention and therapy

---

Edited by  
Kinam Park



# WP

WOODHEAD  
PUBLISHING



Oxford Cambridge Philadelphia New Delhi

Published by Woodhead Publishing Limited,  
80 High Street, Sawston, Cambridge CB22 3HJ, UK  
www.woodheadpublishing.com  
www.woodheadpublishingonline.com

Woodhead Publishing, 1518 Walnut Street, Suite 1100,  
Philadelphia, PA 19102-3406, USA

Woodhead Publishing India Private Limited, 303 Vardaan House, 7/28 Ansari Road,  
Daryaganj, New Delhi – 110002, India  
www.woodheadpublishingindia.com

First published 2013, Woodhead Publishing Limited

© Woodhead Publishing Limited, 2013. The publisher has made every effort to ensure that permission for copyright material has been obtained by authors wishing to use such material. The authors and the publisher will be glad to hear from any copyright holder it has not been possible to contact.

The authors have asserted their moral rights.

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. Reasonable efforts have been made to publish reliable data and information, but the authors and the publisher cannot assume responsibility for the validity of all materials. Neither the authors nor the publisher, nor anyone else associated with this publication, shall be liable for any loss, damage or liability directly or indirectly caused or alleged to be caused by this book.

Neither this book nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming and recording, or by any information storage or retrieval system, without permission in writing from Woodhead Publishing Limited.

The consent of Woodhead Publishing Limited does not extend to copying for general distribution, for promotion, for creating new works, or for resale. Specific permission must be obtained in writing from Woodhead Publishing Limited for such copying.

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

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library.

Library of Congress Control Number: 2013949898

ISBN 978-0-85709-664-7 (print)

ISBN 978-0-85709-676-0 (online)

ISSN 2049-9485 Woodhead Publishing Series in Biomaterials (print)

ISSN 2049-9493 Woodhead Publishing Series in Biomaterials (online)

The publisher's policy is to use permanent paper from mills that operate a sustainable forestry policy, and which has been manufactured from pulp which is processed using acid-free and elemental chlorine-free practices. Furthermore, the publisher ensures that the text paper and cover board used have met acceptable environmental accreditation standards.

Typeset by Newgen Knowledge Works Pvt Ltd, India

Printed by Lightning Source

# Biomaterials for cancer therapeutics

## **Related titles:**

*Drug-device combination products*  
(ISBN 978-1-84569-470-8)

*Nanomedicine*  
(ISBN 978-0-85709-233-5)

*Biomedical hydrogels*  
(ISBN 978-1-84569-590-3)

Details of these books and a complete list of titles from Woodhead Publishing can be obtained by:

- visiting our web site at [www.woodheadpublishing.com](http://www.woodheadpublishing.com)
- contacting Customer Services (e-mail: [sales@woodheadpublishing.com](mailto:sales@woodheadpublishing.com); fax: +44 (0) 1223 832819; tel.: +44 (0) 1223 499140 ext. 130; address: Woodhead Publishing Limited, 80, High Street, Sawston, Cambridge CB22 3HJ, UK)
- in North America, contacting our US office (e-mail: [usmarketing@woodheadpublishing.com](mailto:usmarketing@woodheadpublishing.com); tel.: (215) 928 9112; address: Woodhead Publishing, 1518 Walnut Street, Suite 1100, Philadelphia, PA 19102-3406, USA)

If you would like e-versions of our content, please visit our online platform: [www.woodheadpublishingonline.com](http://www.woodheadpublishingonline.com). Please recommend it to your librarian so that everyone in your institution can benefit from the wealth of content on the site.

We are always happy to receive suggestions for new books from potential editors. To enquire about contributing to our Biomaterials series, please send your name, contact address and details of the topic/s you are interested in to [laura.overend@woodheadpublishing.com](mailto:laura.overend@woodheadpublishing.com). We look forward to hearing from you.

## **The team responsible for publishing this book:**

Commissioning Editor: Laura Overend  
Publications Coordinator: Ginny Mills  
Project Editor: Anneka Hess  
Editorial and Production Manager: Mary Campbell  
Production Editor: Richard Fairclough  
Project Manager: Newgen Knowledge Works Pvt Ltd, India  
Copyeditor: Newgen Knowledge Works Pvt Ltd, India  
Proofreader: Newgen Knowledge Works Pvt Ltd, India  
Cover Designer: Terry Callanan

BP 53, 570 rue de la chimie  
38041 Grenoble Cedex 9, France

E-mail: olivier.renaudet@ujf-  
grenoble.fr

## Chapter 5

H. Kamada and S.-I. Tsunoda\*  
Laboratory of Biopharmaceutical  
Research  
National Institute of Biomedical  
Innovation  
7-6-8 Saito-Asagi  
Ibaraki, Osaka 567-0085, Japan

E-mail: kamada@nibio.go.jp;  
tsunoda@nibio.go.jp

## Chapter 6

H. J. Lee, A. N. Koo, I. K. Kwon, and  
S. C. Lee\*  
Kyung Hee University  
Department of Maxillofacial  
Biomedical Engineering &  
Institute of Oral Biology  
School of Dentistry  
1 Hoegi-dong  
Dongdaemun-gu, Seoul 130-701,  
Republic of Korea

E-mail: schlee@khu.ac.kr

## Chapter 7

R. Zeineldin  
MCPHS University  
Department of Pharmaceutical  
Sciences  
19 Foster Street  
Worcester, Massachusetts 01608,  
USA

E-mail: reema.zeineldin@mcphs.  
edu

## Chapter 8

X. Sun and  
X. Chen\*

Laboratory of Molecular Imaging  
and Nanomedicine (LOMIN)  
National Institute of Biomedical  
Imaging and Bioengineering  
(NIBIB)  
National Institutes of Health (NIH)  
Bethesda, MD 20892, USA

E-mail: shawn.chen@nih.gov

## Chapter 9

C.P. Hollis  
University of Kentucky  
Department of Pharmaceutical  
Sciences  
College of Pharmacy  
789 S. Limestone Street  
Lexington, Kentucky 40536, USA

R. Zhao  
Department of Pharmacy  
Peking University Third Hospital  
Beijing 100191  
China

T. Li\*  
Purdue University  
Department of Industrial and  
Physical Pharmacy  
575 Stadium Mall Drive  
West Lafayette, IN 47907-2091, USA  
E-mail: tonglei@purdue.edu

## Chapter 10

A. L. Lewis  
Biocompatibles UK Ltd. (a BTG  
International group company)  
Farnham Business Park  
Weydon Lane  
Farnham, Surrey, GU9 8QL, UK  
E-mail: andrew.lewis@  
biocompatibles.com

## Chapter 11

G. Shim, M.-G. Kim, J. Y. Park, and  
Y.-K. Oh\*  
College of Pharmacy  
Seoul National University  
Daehak-dong  
Seoul 151-742, Republic of Korea  
E-mail: ohyk@snu.ac.kr

## Chapter 12

D. Needham  
Department of Mechanical  
Engineering and Material  
Science  
Duke University  
Durham, NC 27705, USA  
and  
University of Southern Denmark  
DK-5230 Odense M, Denmark  
E-mail: d.needham@duke.edu

## Chapter 13

A. Wei\*, M. Thomas, J.G. Mehtala  
and J.X. Wang  
Department of Chemistry  
Purdue University

560 Oval Drive  
West Lafayette, IN 47907-2084,  
USA

E-mail: alexwei@purdue.edu

## Chapter 14

A. Singh, A. K. Iyer and M. Amiji\*  
Department of Pharmaceutical  
Sciences,  
School of Pharmacy,  
Northeastern University,  
Boston, MA 02115, USA

E-mail: m.amiji@neu.edu

S. Ganta  
Nemucore Medical Innovations,  
55 Union Street  
Worcester, MA 01608, USA

## Chapter 15

R. Bellamkonda\*  
Wallace H Coulter Department of  
Biomedical Engineering  
Georgia Institute of Technology/  
Emory University School of  
Medicine  
313 Ferst Drive  
Atlanta, Georgia 30332-0535, USA

E-mail: ravi@gatech.edu

K. McNeeley and  
J. G. Lyon  
Wallace H Coulter Department of  
Biomedical Engineering  
Neurological Biomaterials  
and Cancer Therapeutics  
Laboratory

Georgia Institute of Technology/  
Emory University School of  
Medicine  
Atlanta, Georgia 30332, USA

## Chapter 16

C. S. Shin, B. Kwak, B. Han, K.  
Park and A. Panitch\*  
Weldon School of Biomedical  
Engineering  
Purdue University  
206 S Martin Jischke Drive  
West Lafayette, IN 47907-2, USA  
E-mail: [apanitch@purdue.edu](mailto:apanitch@purdue.edu)

## Chapter 17

L. Zhang  
Department of Chemistry  
Brown University,  
Providence, Rhode Island 02912,  
USA

T. Webster\*  
Department of Chemical  
Engineering and Program in  
Bioengineering  
Northeastern University,  
Boston, Massachusetts 02115, USA  
E-mail: [th.webster@neu.edu](mailto:th.webster@neu.edu)



- 17 **Biomaterials for treating skin loss**  
*Edited by D. P. Orgill and C. Blanco*
- 18 **Biomaterials and tissue engineering in urology**  
*Edited by J. Denstedt and A. Atala*
- 19 **Materials science for dentistry**  
*B. W. Darvell*
- 20 **Bone repair biomaterials**  
*Edited by J. A. Planell, S. M. Best, D. Lacroix and A. Merolli*
- 21 **Biomedical composites**  
*Edited by L. Ambrosio*
- 22 **Drug–device combination products**  
*Edited by A. Lewis*
- 23 **Biomaterials and regenerative medicine in ophthalmology**  
*Edited by T. V. Chirila*
- 24 **Regenerative medicine and biomaterials for the repair of connective tissues**  
*Edited by C. Archer and J. Ralphs*
- 25 **Metals for biomedical devices**  
*Edited by M. Ninomi*
- 26 **Biointegration of medical implant materials: science and design**  
*Edited by C. P. Sharma*
- 27 **Biomaterials and devices for the circulatory system**  
*Edited by T. Gourlay and R. Black*
- 28 **Surface modification of biomaterials: methods analysis and applications**  
*Edited by R. Williams*
- 29 **Biomaterials for artificial organs**  
*Edited by M. Lysaght and T. Webster*
- 30 **Injectable biomaterials: Science and applications**  
*Edited by B. Vernon*
- 31 **Biomedical hydrogels: Biochemistry, manufacture and medical applications**  
*Edited by S. Rimmer*
- 32 **Preprosthetic and maxillofacial surgery: Biomaterials, bone grafting and tissue engineering**  
*Edited by J. Ferri and E. Hunziker*
- 33 **Bioactive materials in medicine: Design and applications**  
*Edited by X. Zhao, J. M. Courtney and H. Qian*
- 34 **Advanced wound repair therapies**  
*Edited by D. Farrar*
- 35 **Electrospinning for tissue regeneration**  
*Edited by L. Bosworth and S. Downes*
- 36 **Bioactive glasses: Materials, properties and applications**  
*Edited by H. O. Ylänen*

- 37 **Coatings for biomedical applications**  
*Edited by M. Driver*
- 38 **Progenitor and stem cell technologies and therapies**  
*Edited by A. Atala*
- 39 **Biomaterials for spinal surgery**  
*Edited by L. Ambrosio and E. Tanner*
- 40 **Minimized cardiopulmonary bypass techniques and technologies**  
*Edited by T. Gourlay and S. Gunaydin*
- 41 **Wear of orthopaedic implants and artificial joints**  
*Edited by S. Affatato*
- 42 **Biomaterials in plastic surgery: Breast implants**  
*Edited by W. Peters, H. Brandon, K. L. Jerina, C. Wolf and V. L. Young*
- 43 **MEMS for biomedical applications**  
*Edited by S. Bhansali and A. Vasudev*
- 44 **Durability and reliability of medical polymers**  
*Edited by M. Jenkins and A. Stamboulis*
- 45 **Biosensors for medical applications**  
*Edited by S. Higson*
- 46 **Sterilisation of biomaterials and medical devices**  
*Edited by S. Lerouge and A. Simmons*
- 47 **The hip resurfacing handbook: A practical guide to the use and management of modern hip resurfacings**  
*Edited by K. De Smet, P. Campbell and C. Van Der Straeten*
- 48 **Developments in tissue engineered and regenerative medicine products**  
*J. Basu and J. W. Ludlow*
- 49 **Nanomedicine: technologies and applications**  
*Edited by T. J. Webster*
- 50 **Biocompatibility and performance of medical devices**  
*Edited by J.-P. Boutrand*
- 51 **Medical robotics: minimally invasive surgery**  
*Edited by P. Gomes*
- 52 **Implantable sensor systems for medical applications**  
*Edited by A. Inmann and D. Hodgins*
- 53 **Non-metallic biomaterials for tooth repair and replacement**  
*Edited by P. Vallittu*
- 54 **Joining and assembly of medical materials and devices**  
*Edited by Y. (Norman) Zhou and M. D. Breyen*
- 55 **Diamond-based materials for biomedical applications**  
*Edited by R. Narayan*
- 56 **Nanomaterials in tissue engineering: Fabrication and applications**  
*Edited by A. K. Gaharwar, S. Sant, M. J. Hancock and S. A. Hacking*
- 57 **Biomimetic biomaterials: Structure and applications**  
*Edited by A. J. Ruys*

- 58 **Standardisation in cell and tissue engineering: Methods and protocols**  
*Edited by V. Salih*
- 59 **Inhaler devices: Fundamentals, design and drug delivery**  
*Edited by P. Prokopovich*
- 60 **Bio-tribocorrosion in biomaterials and medical implants**  
*Edited by Y. Yan*
- 61 **Microfluidic devices for biomedical applications**  
*Edited by X.-J. James Li and Y. Zhou*
- 62 **Decontamination in hospitals and healthcare**  
*Edited by J. T. Walker*
- 63 **Biomedical imaging: Applications and advances**  
*Edited by P. Morris*
- 64 **Characterization of biomaterials**  
*Edited by M. Jaffe, W. Hammond, P. Tolia and T. Arinze*
- 65 **Biomaterials and medical tribology**  
*Edited by J. Paolo Davim*
- 66 **Biomaterials for cancer therapeutics: Diagnosis, prevention and therapy**  
*Edited by K. Park*
- 67 **New functional biomaterials for medicine and healthcare**  
*E. P. Ivanova, K. Bazaka and R. J. Crawford*
- 68 **Porous silicon for biomedical applications**  
*Edited by H. A. Santos*
- 69 **A practical approach to spinal trauma**  
*Edited by H. N. Bajaj and S. Katoch*
- 70 **Rapid prototyping of biomaterials: Principles and applications**  
*Edited by R. Narayan*
- 71 **Cardiac regeneration and repair Volume 1: Pathology and therapies**  
*Edited by R.-K. Li and R. D. Weisel*
- 72 **Cardiac regeneration and repair Volume 2: Biomaterials and tissue engineering**  
*Edited by R.-K. Li and R. D. Weisel*
- 73 **Semiconducting silicon nanowires for biomedical applications**  
*Edited by J. L. Coffey*
- 74 **Silk for biomaterials and tissue engineering applications**  
*Edited by S. Kundu*
- 75 **Novel biomaterials for bone regeneration: Novel techniques and applications**  
*Edited by P. Dubrue and S. Van Vlierberghe*
- 76 **Biomedical foams for tissue engineering applications**  
*Edited by P. Netti*
- 77 **Precious metals for biomedical applications**  
*Edited by N. Baltzer and T. Copponnex*

**78 Bone substitute biomaterials**

*Edited by K. Mallick*

**79 Regulatory affairs for biomaterials and medical devices**

*Edited by S. Amato and R. Ezzell*

**80 Joint replacement technology Second edition**

*Edited by P. A. Revell*

**81 Computational modelling of biomechanics in the musculoskeletal system: Tissues, replacements and regeneration**

*Edited by Z. Jin*

**82 Biophotonics for medical applications**

*Edited by I. Meglinski*

**83 Modelling degradation of bioresorbable polymeric medical devices**

*Edited by J. Pan*

Treating cancers is all about delivering an anticancer agent to target cancer cells. It would be best if most, if not all, anticancer agents were delivered to the target cells. Although much more research is necessary to achieve such a goal, current drug delivery systems are able to deliver more drug to the target than ever before. The targeted drug delivery requires the use of various biomaterials, i.e., anything other than the drug itself, to develop various formulations. The role of biomaterials may range from dissolving poorly soluble anticancer drugs to targeted delivery of a drug and an imaging agent simultaneously. Significant progress has been made in developing various delivery systems for anticancer drugs, especially during the last decade with the advent of nanotechnology. While biomaterials with various capabilities have been developed to provide options for treating cancers, their applications in clinical trials have not met with desired clinical outcomes. Developing new biomaterials is no doubt important, but using them properly for the maximum benefit is more important. Since the ultimate goal of developing drug delivery systems is to cure diseases, i.e., cancer in this case, it is necessary to examine the current approaches in light of their potential in controlling tumors in humans. This book is designed to provide collective information on the current approaches used in treating cancers with a focus on biomaterials.

More than a decade has passed since the nanotechnology revolution began, and it has resulted in a great stride toward treating cancers. Drug delivery systems are recently much more than simply dissolving poorly soluble anticancer agents. The properties of nanosized delivery systems can be controlled to respond to environmental factors, in particular temperature or pH changes, selectively releasing a drug at a predetermined site of the body. Despite highly controllable properties of the smart biomaterials, their applications in humans have shown less than expected results. Thus, one of the goals of this book is to provide a careful assessment of the current drug delivery systems, so that the scientists can move forward to achieve the goal of treating cancer more effectively.

I have travelled to different countries to attend various scientific meetings on drug delivery systems. One of the most popular topics for the last

decade has been nanoparticle formulations for targeted drug delivery, usually to tumors. Whenever I talk to a younger generation of scientists, there seems to be a misunderstanding that somehow nanoparticles can cure cancer. It is indeed the hope and goal of the nanotechnology initiative. The reality, however, is that the advances in the last decade in nanotechnology have only produced a basis for making better drug delivery systems. Without understanding the limitations of nanotechnology and the properties of the biomaterials associated with nanotechnology-based formulations, progress toward curing cancer will take detours, consuming more time and more resources. The chapters of this book describe the potentials and the limitations of various approaches that have been developed in cancer therapeutics.

This book is structured to start with a brief introduction on how biomaterials are used in the development of anticancer drug formulations (Chapter 1). Successful treatment of cancer starts with understanding cancer cell biology (Chapter 2) and efficient targeted drug delivery to cancer cells (Chapter 3). Preventing disease is probably the ideal mode of treatment, and carbohydrate-based vaccines against cancers are described in Chapter 4. This is followed by the production of bioactive proteins (Chapter 5) and synthetic polymers (Chapter 6). The next section deals with nanotechnology used for cancer diagnosis (Chapter 7), cancer cell imaging and theranosis (Chapter 8), nanocrystals for maximizing the drug loading (Chapter 9), biomaterials used to block blood supply to tumors (Chapter 10), and siRNA-based therapy (Chapter 11). This section also contains the most recent information on temperature-sensitive liposomes used in clinical studies (Chapter 12) and on gold nanoparticles (Chapter 13). Chapter 14 describes the use of multifunctional nanoparticles to maximize the diagnosis and therapy of cancer. The last section deals with how biomaterials can be used to modulate cancers (Chapter 15) and to develop 3-dimensional tumour models (Chapter 16). The last chapter (Chapter 17) describes the control of cancer cells through controlling the surface nanotopography.

It has been a great pleasure working with the authors of this book. They have been most gracious, first of all, in taking time off from their busy schedules to write the chapters. The authors who participated in this book are those who are sought after by many journal and book editors for their expertise, consequently having limited spare time. Yet all of the authors submitted their chapters in a timely manner to make this book possible. My thanks also go to Laura Overend, the Commissioning Editor, as well as Anneka Hess and Ginny Mills, Publications Coordinators, who handled all administrative activities necessary for the book in a highly professional manner. Finally, I would like to thank the National Institutes of Health for its support on our research projects which always improve our understanding on targeted drug

delivery to tumors, and the Ralph W. and Grace M. Showalter Research Trust Fund, which has allowed me to set aside time for free thinking and for meeting many fellow scientists throughout the world. Real progress is made faster when we communicate the same goal of curing cancer and are ready to compromise our approaches based on the data. If this book serves as a tool for such communication, it has achieved its goal.

*Kinam Park*  
*Purdue University*





# Contents

---

<i>Contributor contact details</i>	<i>xii</i>
<i>Woodhead Publishing Series in Biomaterials</i>	<i>xvi</i>
<i>Preface</i>	<i>xxi</i>
<b>Part I    Fundamentals of biomaterials for cancer therapeutics</b>	<b>1</b>
<b>1        Introduction to biomaterials for cancer therapeutics</b>	<b>3</b>
B. K. LEE, Y. H. YUN and K. PARK, Purdue University, USA and M. STUREK, Indiana University School of Medicine, USA	
1.1      Introduction	3
1.2      Biomaterials used in cancer therapeutics	4
1.3      Materials used in anticancer formulations	5
1.4      Conclusion and future trends	13
1.5      References	13
<b>2        Cancer cell biology</b>	<b>20</b>
R. MRSNY, University of Bath, UK	
2.1      Introduction	20
2.2      Public perception and misunderstanding of cancer cell activity	21
2.3      The 'War on Cancer'	21
2.4      The genetic basis of cancer	24
2.5      Cancer interface with the environment	26
2.6      Cancer cells as moving targets	26
2.7      Conclusion and future trends	28
2.8      References	29