Edited by Felix Kratz, Peter Senter
and Henning Steinhagen

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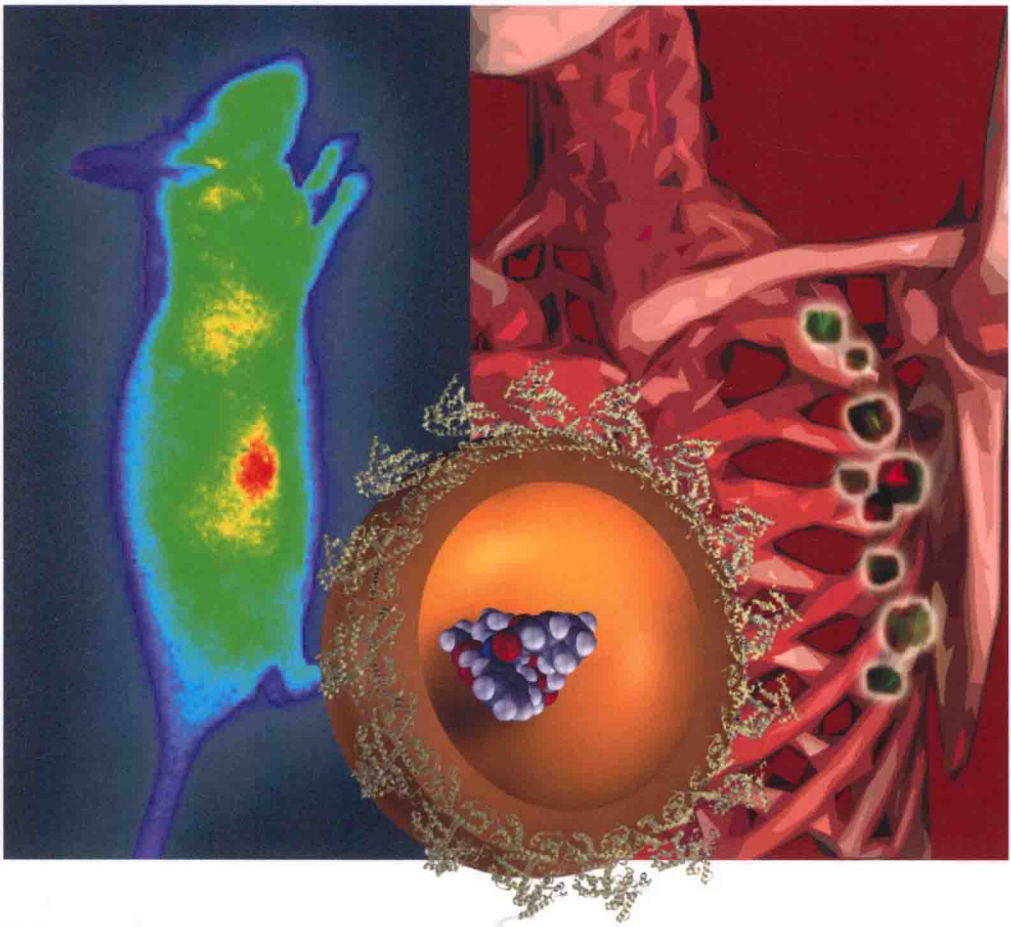
Drug Delivery in Oncology

From Basic Research to Cancer Therapy

Volume 2



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Foreword

It is highly likely that the reason our therapies so often fail our patients with cancer is that either (i) those therapies actually never get to their intended targets or (ii) those therapies are "intercepted" by similar targets on normal cells. If we want to understand why many of our therapies fail our patients, and what we can do to possibly remedy those failures, this book *Drug Delivery in Oncology* can help all of us achieve that understanding – and with this book it will be a state-of-the-art understanding.

Drs. Kratz, Senter, and Steinhagen have assembled a respectable breadth of both seasoned and precocious investigators to put together this very special treatise (49 chapters in all). The chapters are well written with basic science, preclinical, and clinical perspectives.

The book begins with a history and the limitations of conventional chemotherapy. Expert discussions of the vascular physiology of tumors that affect drug delivery (and how to defeat those issues) then follow. There are excellent discussions of the neonatal Fc receptor, development of cancer targeted ligands, and antibody-directed enzyme prodrug therapy (ADEPT).

A very special part of this book is the emphasis on tumor imaging. Again, the authors are major experts in this field, which undoubtedly will continue to mature to enable us to document whether or not our therapeutics actually make it to their intended target(s) – and if not, why not.

There are impressive chapters on macromolecular drug delivery systems, including biospecific antibodies, antibody–drug conjugates, and antibody–radionuclide conjugates. Up-to-date discussions of polymer-based drug delivery systems including PEGylation, thermoresponsive polysaccharide-based and even low-density lipoprotein–drug complexes are also presented.

Those with an interest in learning about nano- and microparticulate drug delivery systems can study liposomes to immunoliposomes, to hydrogels, micelles, albumin–drug nanoparticles, and even carbon nanotubes, which are all covered in this book.

Other special delivery systems covered include peptides–drug conjugates, vitamin–drug conjugates, and growth factor–drug conjugates, conjugates of drugs with fatty acids, RNA and RNA interference delivery, and specific targeted organ drug delivery.

As investigators who want to more effectively treat and indeed cure cancer we have many worries. The first of these is that many of our therapeutics just do not make it into the targets in the tumors. This book gives the reader a comprehensive insight into multiple ways to address this problem. A second major worry is that we are losing our pharmacologists who can solve those drug delivery issues. The editors and the authors of this incredible treatise give us comfort that these pharmacologists are alive and well, and thinking as to how they can contribute to getting control of this awful disease.

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Preface

Modern oncology research is highly multidisciplinary, involving scientists from a wide array of specialties focused on both basic and applied areas of research. While significant therapeutic advancements have been made, there remains a great need for further progress in treating almost all of the most prevalent forms of cancer. Unlike many other diseases, cancer is commonly characterized by barriers to penetration, heterogeneity, genetic instability, and drug resistance. Coupled with the fact that successful treatment requires elimination of malignant cells that are very closely related to normal cells within the body, cancer therapy remains one of the greatest challenges in modern medicine.

Early on, chemotherapeutic drugs were renowned for their systemic toxicities, since they poorly distinguished tumor cells from normal cells. It became apparent to scientists within the field that further advancements in cancer medicine would require new-generation drugs that ideally targeted critical pathways, unique markers, and distinguishing physiological traits that were selectively found within the malignant cells and solid tumor masses. Several new areas of research evolved from this realization, including macromolecular-based therapies that exploit impaired lymphatic drainage often associated with solid tumors, antiangiogenesis research to cut the blood supply off from growing tumors, antibody-based strategies that allow for selective targeting to tumor-associated antigens, and new drug classes that attack uniquely critical pathways that promote and sustain tumor growth. A large proportion of both recently approved and clinically advanced anticancer drugs fall within these categories.

Beyond the generation of such drug classes, it has also been recognized that approved cancer drugs could be made more effective and less toxic through delivery and transport technologies that maximize tumor exposure while sparing normal tissues from chemotherapeutic damage. By doing so, existing or highly potent cytotoxic drugs may display improved therapeutic indices. This has attracted considerable attention and has spawned the area of macromolecular-based delivery strategies.

There are few places where those actively engaged in drug delivery or who may wish to enter the field can find the major advancements consolidated in one place. This prompted us to organize the series of books entitled *Drug Delivery in Oncology* comprised of 49 chapters written by 121 internationally recognized

leaders in the field. The work within the book series overviews many of the major breakthroughs in cancer medicine made in the last 10–15 years and features many of the chemotherapeutics of the future. Included among them are recombinant antibodies, antibody fragments, and antibody fusion proteins as well as tumor-seeking ligands for selective drug delivery and tumor imaging, and passive targeting strategies using macromolecules and nano- and microparticulate systems.

One of the special distinguishing features of this series is that the chapters are written for novices and experts alike. Each chapter is written in a style that allows interested readers to not only to find out about the most recent advancements within the field being discussed, but to actually see the data in numerous illustrations, photos, graphs, and tables that accompany each chapter.

None of this would have been possible without the devoted efforts of the contributing authors, all of whom shared the common goal of creating a new series of books that would provide an important cornerstone in the modern chemotherapeutic treatment of cancer. We are all very thankful for their efforts.

We also wish to thank the publishing team at Wiley-VCH in Weinheim, Germany. In particular, we want to give our wholehearted thanks and kind acknowledgments to Frank Weinreich, Gudrun Walter, Bernadette Gmeiner, Claudia Nußbeck, Hans-Jochen Schmitt, and Ina Wiedemann, who were always helpful and supportive during the 2 years it took to put all this together. It is our hope that this series will provide readers with inspired ideas and new directions for research in drug delivery in oncology.

July 2011

Felix Kratz
Peter Senter
Henning Steinhagen

Contents to Volume 1

Contents to Volume 2