Preface

Cancer therapy has been a major challenge since most of the medicines currently on the market display limited efficacy and/or significant toxicity. Even if new molecules are discovered to treat cancer diseases, the clinical use and efficacy of conventional chemotherapeutics are, indeed, hampered by drug resistance at the tumor level due to physiological barriers (noncellular-based mechanisms), drug resistance at the cellular level (cellular mechanisms), and by non-specific distribution as well as by biotransformation and clearance of anticancer drugs in the body. In other words, conventional chemotherapeutics is often limited to inadequate delivery of therapeutic concentrations to the tumor target tissue or cells. It is therefore of importance to develop new approaches for safer and more efficient delivery of anticancer compounds to tumors both at the cell and tissue level, thereby improving the therapeutic index of these medicines.

In this context, “macromolecular therapeutics” represents, behind the conventional small chemical entities, a second generation of anticancer compounds holding enormous promise and making use of smart approaches to fight cancer. Design and development of macromolecular anticancer therapeutics have assembled interdisciplinary efforts from scientists belonging to various fields like biochemistry, immunology, cell biology, chemistry, bioengineering, pharmaceutics, pharmacology, and oncology. Macromolecular anticancer therapeutics represents a significant volume of research in the recent years so that a large number of macromolecular therapeutic substances are already in the market or are currently in clinical trials or in pre-clinical stage, demonstrating activity against numerous experimental cancer models. Thus, the therapeutic index of various anticancer substances may be increased by linkage with macromolecules of different nature (i.e., proteins, lipids) in order to improve pharmacokinetic and biodistribution. Other anticancer macromolecules are active per se: by mimicking Mother Nature, they are able to recognize cancer targets in a highly specific manner (i.e., antibodies or oligonucleotides). It is out of question that macromolecular anticancer therapeutics possesses improved specificity toward cancer tissues whereas in certain circumstances they also can overcome resistance which, as stated before, is an important drawback associated with many of the conventional currently available anticancer substances. Thus, macromolecular anticancer therapeutics opens new prospects in the current therapy of cancer.
This book will describe in great detail the possible ways to improve cancer treatment by using these macromolecular-based therapies which are

(1) by the selective delivery of small molecule drugs to tumors; this is the major challenge in efficient and safe cancer therapy. The capability of macromolecular substances such as polymers and lipids to alter the fate of conjugated small molecule drugs in the biological environment has prompted the development of macromolecular prodrugs. Thus, a variety of such macromolecular entities have successfully improved the biological fate of the conjugated small molecules and positively contributed toward improvement of efficacy in the treatment of drug-sensitive and drug-resistant tumors, simultaneously lowering the associated toxicity;

(2) by the employment of tumor-specific antibodies, tumors can be targeted with high molecular recognition and efficient therapy can be assured;

(3) by using synthetic fragments of DNA or RNA (i.e., antisense oligonucleotides, aptamers, or small interfering RNA), it is possible to inhibit oncogene expression.

Practically and in order to discuss these various therapeutic strategies, this book containing 17 chapters is divided into 6 parts.

In Part I, the anticancer drugs have been classified, and the various signal transduction pathways involved in the cancer growth and resistance to therapy are discussed. Different classes of anticancer therapeutics either in preclinical or in clinical phases have also been elaborated.

Parts II and III describe the different categories of macromolecular therapeutics of polymer and lipid origin, respectively, designed to improve the accumulation of anticancer agents into tumors by virtue of their physicochemical and pharmacokinetic properties. Design and development, opportunities and challenges, current status, and preclinical and clinical progress of these macromolecular prodrugs are detailed.

Part IV discusses the antibody-mediated drug targeting to cancer employing antibody–drug conjugates, radioimmunoconjugates, toxin–antibody conjugates, antibody-mediated enzyme prodrug therapeutics, and using also antibodies themselves to interfere with specific molecular targets responsible for tumor growth and progression. This part principally deals with the design, the development, the preclinical and clinical status, as well as the challenges involved in cancer therapy using various categories of antibody-based therapeutics.

Part V refers to a variety of therapeutic anticancer oligonucleotides designed and developed for specific inhibition of oncogenes. Their efficacy is discussed both at the pre-clinical and clinical state.

Part VI primarily deals with the molecular therapeutic interventions in breast cancer treatment.

On the whole, this book assembles all the major areas related to the use of macromolecular strategies for cancer therapy and it discusses the “past, present, and future” of these pharmacological approaches. This book is expected to serve
as an essential reference to a broad scientific community including chemists, biologists, biomedical scientists, pharmacologists and pharmaceutical technologists, and oncologists.

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