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Preface

Cancer nanotechnology☆

Nanomaterials, nanoparticles, and nano-devices have been recently added to the arsenal of tools used in cancer research and oncology. Cancer statistics are improving slowly, however fundamental treatment strategy has not changed significantly over the past 30 years and it still relies on surgical resection of the tumor, followed by chemotherapy and/or radiation. Thus, cancer researchers and practicing oncologists are on a quest for new approaches to improve disease intervention outcomes.

Medical nanotechnology possesses attractive characteristics — it facilitates organ-selective drug delivery and enables diverse range of diagnostic tools. On one hand, many of the approaches enabled by it are evolutionary — nanoparticle-based delivery has demonstrated beneficial modification of delivery profiles for several established chemotherapeutics and resulted in reduced side effects. A handful of nanoparticle-based formulations based on these strategies have already been approved by the FDA. On the other hand, new applications solely enabled by nanotechnology are also emerging. For example, a systemic delivery of siRNA, which is becoming an important tool in cancer therapy, is very difficult to achieve without using nanoparticles due to siRNA deterioration in contact with blood and its rapid removal from circulation. The effective delivery of siRNA allows for a significant increase in number of targets, which can be effectively treated, and opens an entirely new class of therapeutics. The opportunities do not stop there, nanoparticles can also be used to broaden therapeutic index of drugs, which have been too toxic to be delivered in free format, and allow their safer delivery.

In vitro nanotechnology-based devices and systems are becoming instrumental to early and precise diagnosis. They are capable of recognizing disease-specific biomarkers with high sensitivity and specificity and can do that for several markers at a time to analyze large panels of genomic or proteomic signatures. The analysis of this data can establish correlations among different biomarker levels and map correlations of network signaling and thus provide tools for patient stratification based on their response to different treatments and ultimately improve therapeutic efficacy of the selected one. Finally, multi-functionality of nanoparticle constructs can be explored to design structures, which facilitate delivery of more than one drug molecule at a time and produce combination therapies, perform multi-modality imaging, or operate in theranostics space through the design of particles simultaneously providing diagnostic and therapeutic capabilities.

Many of these advances are occurring due to the nature of *cancer nanotechnology* field — it is a multi-disciplinary endeavor which leverages knowledge and innovation from several disciplines ranging from materials science and physics to cancer biology and clinical practice. It allows researchers from these disparate communities to contribute their diverse knowledge, experience, and creativity into a final goal of designing a better drug or better diagnostic tool.

The special issue of *Advanced Drug Delivery Reviews*, which you are receiving, focuses on recent advances in this emerging field and presents a collection of several manuscripts, which discuss nanotechnology-enabled drug delivery at length, but also cover diagnostic and intra-operative imaging applications to demonstrate multi-faceted impact of nanotechnology on cancer.

Two papers by Bertrand and Farokhzad and Biswas and Torchilin provide a thorough overview of several factors contributing to effective nanoparticle-mediated delivery. Fundamentals of Enhanced Permeability and Retention (EPR) effect, believed to be responsible for nanoparticle accumulation in tumor, value of active targeting and their correlation with nanoparticle size, shape, and surface properties is discussed and supported with several examples of nanoconstructs in pre-clinical and clinical development. Torchilin's paper discusses in detail intracellular uptake and strategies enabling effective endosomal drug escape and delivery to specific organelles. Cheng and Lesniak's paper deals with novel therapies for brain cancer and shows opportunities for design of nanoparticles capable of crossing blood–brain barrier and strategies coupling a contrast agent and a therapeutic agent into one to produce theranostic constructs. Li and Lam's contribution outlines importance of designing nanoparticle delivery vehicles capable of responding to multiple stimuli for controlled drug release in complicated *in vivo* microenvironments. Shu and Guo's manuscript takes a different approach to nanoparticle design and shows that RNA can be folded into nanoparticle-like constructs, exhibit therapeutic properties and show desirable biodistribution characteristics. Hussain and Nquyen introduce an emerging field of intra-operative imaging and describe feasibility of using molecular imaging techniques to delineate tumor margins for more accurate surgical removal. Muluneh and Issadore discuss NMR-based devices capable of *in vitro* detection of circulating tumor cells and proteins from blood and use of these devices to diagnose the disease and monitor effectiveness of therapy. Finally, Ozpolat and Lopez-Berestein review siRNA-based therapeutics and various nanoparticle options to their effective delivery.

The set of manuscripts from outstanding investigators included in this special issue provides for an excellent read on the current state-of-the-art capabilities of cancer nanotechnology and future opportunities of the field is promising.

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