Preface

Significant progress in the fundamental understanding of cancer as well as its detection and treatment has been made by both the research and clinical communities over the past several decades. As a result, the death rates of many cancers are on the decline. However, despite tremendous efforts by many, much still remains to be understood about this highly heterogeneous and complex disease, from why cancers progress so differently in each individual patient to why each patient reacts differently to cancer treatments. In order to effectively treat every patient, advanced precision solutions are needed that can discern and contend with such heterogeneities, even those at the cellular and genetic levels. In order to give the patient the best chance for survival, their cancer must be detected early, when it has not yet metastasized, and treated using personalized options that are highly effective, noninvasive, biocompatible, and targeted and that do not cause significant unwanted immediate or long-term side effects. It would be ideal if such precision therapeutics could induce cancer regression and at the same time track its effect on the disease state in real-time. Many of the current solutions fall short of achieving many of these requirements, leaving room for additional research and innovation by scientists and physicians alike.

The field of nanoscience and technology is offering up myriad tools and materials that have the potential to dramatically impact cancer research, diagnostics, and treatment. The chemical and physical properties of nanostructures are highly dependent upon their size, shape, and composition. Therefore, the architecture of nanostructures can be tuned during synthesis or via post-synthetic modification techniques to produce materials with the desired properties for a given application, biomedical or otherwise. Indeed, nanoconstructs are highly modular, allowing them to be designed and synthesized with multiple functionalities in mind. This means that a single nanoconstruct can be used as a modality for cancer therapy, detection, and/or bioimaging tasks simultaneously. In addition, the small size of nanoparticles, which puts them on the same length scale as many biological structures, grants them privileged access to biological systems and tumor microenvironments, often resulting in unique and potentially useful interactions with biological structures. These and other factors have enabled nanostructures to be the cornerstones of new technologies and processes that surpass traditional ones used for the study, detection, and treatment of cancer in terms of their capabilities and efficacies.

A diverse array of nanostructures that have found application within the field of biomedicine, specifically cancer research, detection, and treatment, are highlighted in this book. Many of these nanostructures possess both inorganic and organic or biological components; the properties of such structures are a synergistic combination of each and hence many possess theranostic (combined therapy and detection/imaging) abilities. For example, spherical nucleic acids (SNAs), which are highlighted in Chapters "Nanoflares as Probes for Cancer Diagnostics" and "Therapeutic Applications of Spherical Nucleic Acids", are made by templating a shell of highly oriented oligonucleotides on the surface of an organic or inorganic nanoparticle (e.g., gold, silver, iron oxide, liposomes). These nanomaterials, which can be made from one or more different types of oligonucleotides and modified with fluorophores and other tracking entities, are revolutionizing aspects of the intracellular detection and gene regulation arenas. Magnetic nanostructures (MNS, Chapter "Theranostic Magnetic Nanostructures (MNS) for Cancer"), which can possess cores comprised of iron, nickel, zinc, or cobalt, and nanodiamonds (NDs, Chapter "Nanodiamond-Based Chemotherapy and Imaging"), which have carbon-based cores, have been coated with a variety of small or polymeric molecules and successfully used in drug delivery and magnetic resonance imaging (MRI), among other areas. Lipid-based nanostructures (Chapter "Theranostic Lipid Nanoparticles for Cancer Medicine") have found use as imaging agents in computerized tomography (CT) and positron emission tomography (PET), and they can also be used in photothermal (PT) and photodynamic (PD) therapy applications. High-density lipoprotein (HDL)-like nanostructures can be used to precisely target lymphoma cells and to deliver a variety of therapeutic cargos, including small molecule drugs and siRNA, in a highly specific manner (Chapter "Synthetic High-Density Lipoprotein-Like Nanoparticles as Cancer Therapy"). Nanoparticles of gold or iron are being used as radiosensitizers (Chapter "Radiosensitization and Nanoparticles") to enhance the effects of radiation on tumor cells via DNA damage and hyperthermia. Finally, the porosities of hybrid particles that are comprised of metal-organic frameworks (MOF) and polysilane moieties have been used as carriers for cancer imaging and therapeutic agents (Chapter "Hybrid Nanoparticles for Cancer Imaging and Therapy").

Many of these nanomaterials have found a unique place in biology and medicine, and some are available in the marketplace. Spherical nucleic acid (SNA) nanoconstructs (Chapters "Nanoflares as Probes for Cancer Diagnostics" and "Therapeutic Applications of Spherical Nucleic Acids") were first invented in 1996 and have since been commercialized extensively. Indeed, there are now over 1,800 products and a robust pipeline of therapeutic lead compounds that exist based upon SNAs. For example, SmartFlares™, commercialized by EMD Millipore and AuraSense, LLC, are changing the way circulating tumor cells (CTCs) are tracked and studied by providing the only way to sort live cells based on intracellular genetic and small molecule markers (Chapter "Nanoflares as Probes for Cancer Diagnostics"); SNAs are also important lead structures for the treatment of cancers, including those of the brain (glioblastoma multiforme) and skin (Chapter "Therapeutic Applications of Spherical Nucleic Acids"). Likewise, nanodiamonds

(Chapter "Nanodiamond-Based Chemotherapy and Imaging"), due to their unique surface properties, are becoming a popular platform for theranostic and chemotherapeutic applications. These structures are currently being validated in nonhuman primate/large animal studies and the first in-human clinical trials are being planned.

However, despite the almost limitless potential of nanostructures and the significant progress that has been made thus far, many questions still remain. For instance, intense research is currently being undertaken to understand how nanoparticles interact with biological environments, including cancer cells, from how they pass through the tumor microenvironment (Chapter "Exploring the Tumor Microenvironment with Nanoparticles") and enter cancer cells to how they escape from the endosome and are ultimately exocytosed (Chapter "How Nanoparticles Interact with Cancer Cells"). One major consideration in this process is the nature and formation of the "protein corona" (Chapter "Engineering the Nanoparticle-Protein Interface for Cancer Therapeutics"), a protein accumulation layer that forms on the surface of colloidal particles in biological environments, including blood and serum. This corona can change the effective structure of the nanoconstruct, and accordingly its behavior and interactions with biological systems important in cancer research and treatment. So that the effect of each individual architectural parameter on the system can be isolated, it is important to develop materials that are truly "calibration-quality" (Chapter "Calibration-Quality Cancer Nanotherapeutics"). The particle replication in non-wetting templates (PRINT®) process is one method that can be used to fabricate polymer-based nanoparticles with independent control over each particle parameter for this purpose.

Given the progress that has been made in the past ten years, we are optimistic that the next decade will bring about more exciting advances in the area of cancer nanotechnology. A growing number of nanostructures and processes will complete the often lengthy and complicated US Food and Drug Administration (FDA) approval phase (Chapter "Cancer Nanotherapeutics in Clinical Trials") and enter the clinic where they can be used to save lives and contribute positively to humanity.

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