Chapter 11
Receptor-Based Combinatorial Nanomedicines:
A New Hope for Cancer Management

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ABSTRACT

Nanotechnology-based drug-delivery systems, as an anticancer therapy tool, have shown significant potentials for the diagnosis and treatment of cancer. Recent studies have demonstrated that cancer therapy could be efficiently achieved by combinatorial therapies, approaches using multiple drug regimens for targeting cancers. However, their usages have been limited due to shorter half-lives of chemotherapeutic agents, insignificant targetability to tumor sites and suboptimal levels of co-administered conventional drug moieties. Thus, nanotechnology-based drug-delivery systems with effective targetability have played a crucial role to overcome the limitations and challenges associated with conventional therapies and also have provided greater therapeutic efficacy. Herein, the authors have focused on various drug-incorporated combinatorial nanocarrier systems, the significance of various receptors-associated strategies, and various targeted delivery approaches for chemotherapeutic agents.

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INTRODUCTION

The National Nanotechnology Initiative has defined nanotechnology as the process of designing, synthesizing, characterizing, and using the materials and devices that have dimensions in the nano range scale (10-200 nm) (National Science and Technology Council Committee on Technology., 2005). Generally, nanomedicines are the fabrication of active pharmaceutical ingredients or materials for disease treatment and diagnostic purposes in the nanoscale range (Sanna et al., 2014). Nowadays, nanomedicine-based delivery systems are getting a lot of attention as they have been used to develop various approaches in delivering medications, particularly chemotherapeutics, with significant safety and efficacy. Formulation scientists have developed a diverse class of nanoparticles (NPs), demonstrated their various applications in drug delivery, observed their effects over the cellular intracellular uptake, biodistribution and dosing efficacy of incorporated drug regimen and also noticed their targetability at diseased sites rather affecting the healthy or normal cells (Farokhzad et al., 2009). A revolutionary change was seen in disease treatment with the application of nanoparticulate-based drug delivery systems. In recent years the Food and Drug Administration (FDA) has approved several liposomes and polymer-based nanoformulations for the clinical purpose (Sanna et al., 2014). The NPs have exhibited tremendous ability to improve the solubility of the drug, execute the process of drug loading and release to the targeted sites in a controlled manner (Chrastina et al., 2011). The NPs have exposed various unique features such as large surface to volume ratio, flexible exterior boundary, biodegradability, low cytotoxicity, and these features have enhanced their applications in establishing nanomedicines. Nanomedicine has also shown fruitful insights into the development and establishment of personalized medicine (Davis et al., 2008; Zhang et al., 2012). Novel NPs-based anticancer therapy symbolizes an innovative and potential drug delivery strategy to conquer the challenges and restrictions of conventional chemotherapeutic agents by improving drug uptake and selective intracellular accumulation in tumor tissues via passive and active targeting with minimal toxicity to normal cells (Blau et al., 2016; Shapira et al., 2011; Bar-Zeev et al., 2017).

The NPs have shown significant applications for developing drug delivery systems (DDSs) incorporated with hydrophobic drugs, improved their solubility, enhanced cellular uptake and targetability at the target sites with no or reduced cytotoxicity. Further such approaches can surmount the drug resistance in malignancy. With this concept, it makes possible to design a rational DDS to target the cancer cells and even establish personalized medicine or therapy. The nanotechnology science has exhibitednumerous potentials including initial recognition of cancer cells, active and passive targeting, improved biocompatibility, and versatility of applying imaging and therapeutic proficiencies in chemotherapy (McNeil., 2009).

Surface-engineered NPs based therapeutics offers several clinical advantages in disease treatment. Polyethylene glycol (PEG) is usually employed for modifying NPs surface, has prevented the clearance of NPs from the blood circulation and thus increased the circulation time and cellular uptake of a drug at the targeted sites (Farokhzad et al., 2009; Chow et al., 2013). The functionalized NPs surface not only enhances the drug efficiency but concurrently minimizes the dosage, and thus provides a unique approach to optimize drug pharmacokinetics (Chow et al., 2013). NPs can deliver the drug to the targeted sites through epithelial or endothelial barriers, in response to the passive and active targeting process (Chrastina et al., 2011). There are few examples of surface-engineered NPs which are designed to overcome challenges and limitations for cancer drug delivery.

The application of the NPs-based approaches has facilitated enhanced drug solubility, minimized cytotoxicity, and better drug pharmacokinetics, an example is Doxil® and Genexol-PM®. In 2006, Noble prize in physiology brought a revolution in the field of gene targeting and silencing, which evolved new