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Polymer Nanostructures Synthesized by Controlled Living Polymerization for Tumor-Targeted Drug Delivery

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Abstract

The development of drug delivery systems based on well-defined polymer nanostructures could lead to significant improvements in the treatment of cancer. The design of these therapeutic nanosystems must account for numerous systemic and circulation obstacles as well as the specific pathophysiology of the tumor. Nanoparticle size and surface charge must also be carefully selected in order to maintain long circulation times, allow tumor penetration, and avoid clearance by the reticuloendothelial system (RES). Targeting ligands such as vitamins, peptides, and antibodies can improve the accumulation of nanoparticle-based therapies in tumor tissue but must be optimized to allow for intratumoral penetration. In this review, we will highlight factors influencing the design of nanoparticle therapies as well as the development of modern controlled “living” polymerization techniques (e.g. ATRP, RAFT, ROMP) that are leading to the creation of sophisticated new polymer architectures with discrete spatially-defined functional modules. These innovative materials (e.g. star polymers, polymer brushes, macrocyclic polymers, and hyperbranched polymers) combine many of the desirable properties of traditional nanoparticle therapies while substantially reducing or eliminating the need for complex formulations.

1. Scope

In recent years, polymeric nanoparticles have joined established liposome technology (e.g. Doxil) as clinically approved anticancer drug delivery vehicles. The first approved formulation, Genexol-PM, a polyethylene glycol-*b*-poly(*D*,*L*-lactide) (PEG-PDLLA) micelle encapsulating paclitaxel, is available in Korea and is undergoing Phase II clinical trials in the US.[1] Several PEG-polypeptide micelle formulations are also in mid- to late-stage clinical trials for delivery of cisplatin, paclitaxel, and doxorubicin,[1] and a targeted micelle formulation for docetaxel delivery (BIND-014) is currently in Phase II trials. These aforementioned micelles are self-assembled structures that mitigate the toxicity profiles and improve solubility of highly hydrophobic drugs. However, ongoing challenges with such systems include the need for a formulation step during