Self-Assembled Nanoparticles for Cancer Imaging and Therapy

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The development of chemotherapeutic agents for the treatment of cancer has resulted in overcoming some tumors. Despite advances in the synthesis of new anti-tumor agents, these compounds possess inevitable, serious side effects like non-specific toxicity that limit the dose and uses of the drug. Attempts to decrease the toxicity of anti-tumor agents to normal tissues have involved localizing cytotoxicity at the tumor site and employing macromolecular pro-drugs to prolong duration of drug activity. Especially, the introduction of the concept "the enhanced permeability and retention (EPR) effect" to the cancer chemotherapy gave rise to extensive researches on polymeric drug carrier.

Tumors have a unique feature which is greatly different from normal tissues. The tumoral angiogenesis renders tumor tissues to display several distinctive characters such as hyper-vasculature defective vascular architecture, and a deficient lymphatic drainage system, which lead macromolecules to be accumulated preferentially and to be retained more in tumor tissues than in normal tissues. The superiority of macromolecular drug carriers to low molecular weight anti-cancer agents is based on this EPR effect.

Another strategy of drug delivery system using the EPR effect is to employ polymeric micelles as long circulating drug carriers. Polymeric amphiphiles with both hydrophilic and hydrophobic groups form self-assemblies composed of an inner core of hydrophobic segments and an outer shell of hydrophilic segments in aqueous media. The hydrophobic core serves as micro-reservoirs for hydrophobic drugs. Hence, drug delivery using polymeric micelles or micelle-forming polymer-drug conjugates has been recognized as an effective strategy for passive tumor targeting.

Additionally, the particle size dependent anti-tumor effect of polymeric micelles is important in increasing the therapeutic value of anti-tumor agent. Because most tumor vessels have an irregular diameter and pore cutoff size, a detail study of the particle size dependent permeability and retention time in tumor site is an important part of cancer therapy. Many polymeric micelles carrier is convenient to use since they have been reported to be suitable for escaping the reticuloendotherial cell system (RES) and renal extraction because of their small particle size that range approximately from 20 to 100 nm. However, many research groups are trying to improve the use of polymeric micelles by overcoming several problems such as low drug entrapment efficiency, short retention

time into the tumor site etc. Thus, the development of a new method to study the tumor specific accumulation and anti-tumor effect of large size aggregates can provide important information about the therapeutic potential of the nanoaggregate.

In this study, to obtain novel amphiphilic polymers that provide potential applications in cancer therapy and imaging, hydrophobically modified glycol chitosans (HGCs) were prepared by covalent attachment of fluorescein isothiocyanate (FITC), doxorubicin, or 5β-cholanic acid. The nanoaggregates composed of hydrophobically modified glycol-chitosan had a large diameter ranging from 150 to 500 nm. The tumor targeting efficiency, biodistribution, tumor imaging, and their anti-tumor effect in a tumor-bearing animal model will be presented.

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