

Drug Design for Cancer: Gold Nanoparticle-Liposome Hybrids for Drug Delivery and Monitoring

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Cancer is a major cause of death worldwide and is on the increase, and its clinical effective therapy remains poor. In the traditional clinical treatment of disease, diagnosis and therapy are two separate processes and also use two independent drugs; therefore, patients often delay the best period of disease therapy for taking two treatments. At present, the most common methods for medical imaging diagnosis are X-ray, tomography, CT, B ultrasound, magnetic resonance and endoscopy. Nevertheless, there are some serious problems, such as the sensitivity of these techniques is low, it is the reason that some early tumor is difficult to find, which bring about the patient losing the best treatment time; in addition, the dose of a drug required to achieve clinically effective cytotoxicity in tumors often causes severe damage to non-malignant cells, producing undesirable side effects. There is a growing need for the designing of novel image agent to allow noninvasive, combinatory therapeutic-diagnostic applications. Recently, a word “theranosis” has been created, combining the words to describe the implementation of these two distinct pursuits simultaneously. Therefore, theranostic agents have received a great deal of research interest in cancer diagnosis and treatment.

Gold nanoparticles are allowed to be used in biological and medical application owing to their good biocompatibility as well as excellent optical and electronic properties. In recent years, Au nanomaterials have attracted greater attention from researchers because it was demonstrated that Au nanomaterials have great potential for cancer photothermal therapy. Gold nanoshells are an excellent candidate for near-infrared irradiation (NIR) light-triggered drug release, which provide an attractive approach for the spatiotemporal control of drug delivery. It may offer precise, on-demand drug delivery within individual cells *in vitro* and precise treatment of cancer *in vivo*. Furthermore, the strong optical absorption of gold nanoshells can rapidly increase the local temperature under NIR to kill selectively tumor cells, not harming normal cells. Tumor cells are very sensitive to heat, and can cause their death. Therefore, the gold nanoshells can be used for tumor photothermal ablation therapy [1].

Liposomes are proven candidates for delivery of a wide range of therapeutics, since hydrophilic drug can be encapsulated in their internal aqueous compartment or hydrophobic one embedded within the phospholipid bilayer. Liposomes have shown some advantages such as higher stability, good biocompatibility, non-toxicity, biodegradability, and controlled release of the encapsulated drug. Especially, the long-circulating liposomes could slowly accumulate in tumor, inflammation or infarcted sites with affected and leaky vasculature via enhanced permeability and retention effect (EPR effect) [2]. Clinical applications of liposomes on the delivery of anticancer agents for the treatment of different cancer are well-established. Liposomes’ permeability is greatly enhanced around the membrane melting temperature (T_m), which depends on the lipid composition. A drug can be released if the liposome membrane is heated above T_m [3].

A novel anticancer drug can be designed, which is Au nanoparticle-liposome hybrids delivery system. The delivery system allows deep

tissue detection, therapy, and monitoring on living body, and the hybrids can be designed by controlling the thickness of the gold shell and the diameter of the core, which realizes that the surface plasmon resonance and the optical absorption of gold nanoshells can be tuned to the NIR to enhance spectral signal in the cytoplasm and obtain the detection signal. Furthermore, when the tunability is designed in the 690-900 nm, the absorption of human tissues is minimal and penetration is optimal, which can reach the tissues under several inches [4]. Therefore, the advantages of gold particle-liposome hybrids are as follows: (1) biodistribution can be controlled by the change of the nanoparticle properties, (2) preservation an effective blood concentration by escaping the removal carried out by the reticuloendothelial system, (3) high potency hydrophobic compounds can be dispersed in water and delivered systemically by nanoparticles, (4) nanoparticles can enhance the level of signal detection for the more sensitive detection of disease.

Gold nanoparticle-liposome hybrids can improve the efficiency of diagnosis by providing better detection signal contrast and biological distribution. These properties make it possible as a new biological contrast agent. Ke et al. successfully constructed gold nanoshelled microcapsules, which can kill HeLa cells *in vitro* by exposure to 808 nm light irradiation. Meanwhile, it also can still maintain adequate acoustic properties that are required to act as an ultrasound contrast agent [5]. The research showed that the liposome release can be initiated within seconds by irradiating hollow gold nanoshells with a NIR pulsed laser. NIR light penetrates into the tissue up to 10 cm, allowing these gold nanoparticle-liposome complexes to be addressed noninvasively within a significant fraction of the human body [6].

The integration of nanotechnology, materials science, pharmacy, and biotechnology is bringing about advances in the medical technologies used for the diagnosis and therapy of cancer, as well as the monitoring of drug distribution. For the success of gold nanoparticle-liposome hybrids nanomedicine, further studies are required. It is also necessary to devise a means of mass and easy producing gold-liposome hybrids, as well as optimizing their dose or concentration, size, flow rate in blood stream and so on. The hybrids have great potential in clinical practice for the purpose of early detection and minimally noninvasive treatment of cancer, and are expected to bring about an improvement

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in the detection accuracy, clinical outcome, and patient quality of life. Meanwhile, the long-term safety of nanodrugs for *in vivo* applications should be confirmed. This is a favorable starting point for anticancer multiple-approach therapy.

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