Commentary

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Apoptotic Sonodynamic Anti-Tumor Nanotherapy Induced Acute Respiratory

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Description

Cancer is a major public-health problem worldwide. More than 30% of all people will develop some form of cancer during their lifetime. For instance, it is the second leading cause of death in the United States, and is expected to surpass heart diseases as the leading cause of death in the next few years. According to the estimation of the most common cancers expected to occur in the United States in 2015, most common cancers among men will be prostate (about one-quarter of new diagnoses cancers), lung and bronchus, and colorectal cancers. The most commonly diagnosed cancers in women will be breast (expected to account for 29% of all new cancers), lung and bronchus, and colorectal. Estimated data of predicted deaths by cancer in the United States for five leading cancer types by gender. Cancer is a complex multistep process where cells attain certain hallmark properties because of both genetic and epigenetic alterations [9] Diagnosis is undoubtedly the first and most important step in cancer therapy. The first therapeutic option for patients with solid tumors is usually surgery, to remove cancer cells.

Afterwards, and to destroy any possible remnants of the tumor, the area should be irradiated. Simultaneously or in a later phase, chemotherapy can be used to kill residual cancer cells and possible metastases. Conventional anticancer therapies are distributed non-specifically in the body and damage both cancer and healthy cells in a state of division. This involves the use of suboptimal treatment to prevent excessive toxicities. Furthermore, many effective drugs are hydrophobic or, if soluble, never reach their destination. Moreover, the multiple and interconnected pathways of carcinogenesis complicate efforts for providing effective therapies. Therefore, a paradigm change is underway as researchers are working to design therapies for specific cancer phenotypes.

While the search for new strategies for cancer therapy continues, it becomes increasingly evident that targeted nanovehicles, designed to achieve the specific organ is the key to formulate effective treatment. The greatest advantage of the application of nanomedicines in cancer lies in its potential to create novel structures with enhanced abilities to translocate through cell membranes, thereby, enhancing their delivery efficiency. The benefits of developing nanoparticles as drug-delivery systems include enhancement of pharmacological activity, delivery of more than one therapeutic agent for combination therapy, solubility —as many drug.

Toxicity of Nanoparticles

We hypothesized that coating nanoparticles with RBC membranes could enable them to evade the phagocytic system by incorporating the “natural” properties of the RBC membrane, thereby achieving a long half-life in the circulation. We further hypothesized that loading these RBC membrane-coated nanoparticles with an antiatherosclerotic compound would treat atherosclerosis more effectively than uncoated nanoparticles. In addition, poly(lactic-co-glycolic) acid (PLGA), a material approved by US food and drug administration (FDA), was selected as an excellent biocompatible and biodegradable material for efficient drug loading. Rapamycin (RAP), an inhibitor of the mammalian target of the rapamycin (mTOR) pathway, has been considered to be an effective antiatherosclerotic agent, in view of its multiple pharmacological activities including anti-inflammation, antimigration, antiproliferation, and autophagy activation.[34,35] Therefore, the PLGA nanoparticles were loaded with RAP as a “core” structure. We then coated the nanoparticles with RBC vesicles (RV), extracted from RBCs, to fabricate the RBC-based “core–shell” structured nanocomplexes. In this study, we have shown that this strategy enhances the half-life of nanoparticles in the circulation. More importantly, we have shown that these biomimetic nanoparticles can accumulate within atherosclerotic plaques and efficiently inhibit the progression of atherosclerosis.

Mechanisms Underlying Nanotoxicity

The cost of preparing carrier-entrapped bioactive molecules can be further reduced by minimising the number of steps and time it takes to produce these formulations into products that are suitable for human or animal use. It is also desirable to have a method capable of producing a vast number of polymer, lipid and surfactant-based carrier complexes in a single step and in a single piece of equipment or vessel, without involving harmful substances or procedures. Indeed, in a recent simple method, that is an improved and further developed version of heating method, different carrier systems (i.e. microspheres, nanospheres, liposomes, VPG, archaeosomes, niosomes, micelles and nanoparticles) can be prepared using a single

apparatus in the absence of potentially toxic solvents in less than an hour. The method is economical and capable of manufacturing bioactive carriers with a superior monodispersity and storage stability using a simple protocol.

Another important feature of the method is that it can be adapted from small to industrial scales. This method is obviously most suitable for production of carrier systems for different in vitro and in vivo applications and involves heating and stirring the carrier ingredients, in the presence of a polyol, at a temperature between 50 to 120 °C (based on the properties of the ingredients and material to be entrapped). Incorporation of bioactives into the carriers can be achieved by several routes including: i) adding the bioactive to the reaction medium along with the carrier ingredients and polyol; ii) adding the bioactive to the reaction medium when temperature has dropped to a point not lower than the transition temperature of the ingredients; and iii) adding the bioactive to the carrier after it is prepared at ambient temperatures (e.g. incorporation of different DNA molecules to micro- and nanocarriers can be achieved by this route.

Following preparation of carrier systems and incorporation of bioactive materials the next issue to be addressed is targeting the formulation to its site of action, which can be inside or outside the body. Examples of in vitro bioactive targeting include delivery of encapsulated antibiotics, to control bacterial growth in systems such as food or pharmaceutical reactors, and cheese-ripening enzymes preferentially in the cheese curd for accelerated ripenning.