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Nanoscaled anticancer therapeutics

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ABSTRACT

Nanoscaled drug delivery platforms have shown promising clinical results in several types of cancer and inflammatory disorders. Targeted therapies are a major focus of cancer treatment. With recent advances of nanotechnology, nanoparticle-based targeted drug delivery, especially for cancer therapies, has attracted increasing attention in the past two decades. The therapeutics-encapsulated nanoparticless approach uses the unique properties of the tumor microenvironment, most notably leaky tumor vasculature, which is highly permeable to nanoparticles relative to normal tissue.

Keywords

Cancer, nanoparticles, therapeutics, drug delivery.

Cancer today is one of the leading causes of mortality across the globe that can affect humans in more than 100 diverse forms. Cancer is caused by the synthetic action of internal and external factors, including genetic mutations, environmental pollution, and unhealthy diet. Early diagnosis has a vital impact on improving disease-free survival and reducing the mortality of cancer patients. The commonly used tool for the diagnosis of cancer is imaging test, which includes CT scans, MRI, X-ray tests, nuclear medicine scans, ultrasound and endoscopy, etc. The cancer management mainly involves surgery, chemotherapy, radiotherapy, and targeted therapy. Surgery is the preferred method for “early-stage” cancers. A high dose of radiation is applied during radiotherapy to kill the cancer cells, and sometimes it is also used in a localized setting, conjointly with surgical procedures. Cytotoxic drugs are used during chemotherapy, which preferentially kill the rapidly dividing cancer cells. On the contrary, “targeted therapy” targets specifically the changes in cancer cells that help in their growth, cell division, and metastasis.

Targeted therapies are a major focus of cancer research today. With recent advances of nanotechnology, nanoparticle-based targeted drug delivery, especially for cancer therapies, has attracted increasing attention in the past two decades. Nanoparticles have several advantages for targeted drug delivery. First, they are small in size and can escape the uptake of mononuclear phagocytic system (MPS) cells in the blood and organs. Second, the advantages of tumor targeting and controlled drug release often result in increased therapeutic efficacy of the antitumor agents, and weakened side effects [1], whereas most free anticancer drugs are taken up nonspecifically by all types of cells, resulting in serious side-effects. In addition, due to their unique size and amenability to surface modification to incorporate the desired characteristics, inorganic and polymer nanoparticles are particularly well-suited for crossing various biological barriers, such as leaky vasculature. Strategies on delivering therapeutics-encapsulated NPs to cancerous tissue have been focused on passive and active targeting. This approach uses the unique properties of the tumor microenvironment, most notably: (i) leaky tumor vasculature, which is highly permeable to macromolecules and nanoparticles relative to normal tissue; and (ii) a dysfunctional lymphatic drainage system, which results in enhanced fluid retention in the tumor interstitial space [2]. As a result of these characteristics, the concentration of polymeric NPs and macromolecular assemblies found in tumor tissues can be up to 100x higher than those in normal tissue [2].

The success in cancer nano-therapy is extremely dependent on the development of carriers that are able to efficiently deliver therapeutic agents to the cytosolic compartment of target cells with minimal toxicity [3]. Among many different types of nanoparticles (NPs) applied for this aim, honeycomb-like porous silicon (HCPSi) NPs show remarkable advantages, including high surface area, stable nanostructure, tunable pore diameter, two functional surfaces (external particle surface and internal pore surface), modifiable shape and size, effective protection of the therapeutic cargos from undesirable degradation, as well as superior safety at concentrations adequate for pharmacological applications [4-6].

Despite the above mentioned advantages, there are still concerns regarding the potential of HCPSiNPs at the cellular level due to the low cellular interaction and entry into the cells [7,8]. In addition, the internalized HCPSiNPs usually become entrapped inside endosomes and ultimately end up in the lysosome, a biological compartment in charge for enzymatic degradation and inactivation of different compounds [9]. Therefore, these nanostructures will possess a high potential for cancer therapy, if rendering the ability to breach cellular membrane and reach the cytoplasm or nucleus of the cell, a difficult task to achieve due to the complexity of the biological barriers [10].

Since many types of developed NPs with favorable physicochemical properties in vitro cannot be successfully applied in vivo owing to the limited intracellular functionality, numerous attempts have been made to find new approaches to attenuate this drawback by enhancing their cellular uptake and endosomal escape [11]. For example, cell penetrating peptides have been widely used for cellular uptake enhancement despite several disadvantages, such as low metabolic stability, possible immunogenicity, and dependency of their membrane translocation ability on the amino acids arrangement and site of conjugation with the NPs [12,13]. To overcome these problems, new alternative strategies are

essential to achieve favorable therapeutic effect for the nanomedicines [14].

SUMMARY

The mentioned delivering therapeutics-encapsulated nanoparticless approach uses the unique properties of the tumor microenvironment, most notably: (i) leaky tumor vasculature, which is highly permeable to nanoparticles relative to normal tissue; and (ii) a dysfunctional lymphatic drainage system, which results in enhanced fluid retention in the tumor interstitial space. Honeycomb-like porous silica nanoparticles show remarkable advantages, including high surface area, stable nanostructure, tunable pore diameter and effective protection of the therapeutic cargos from undesirable degradation,

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