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The Impact of Nanoparticle-Modified Carriers on Drug Entry and Exit in Tumor Cells

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Abstract:

In recent years, malignant tumors have posed a severe threat to human health. Currently, most clinically used drug molecules are non-targeted chemical structure drugs with low bioavailability. The halogens or sulfur elements in their structures can easily cause toxic side effects to normal cells. High doses are required to achieve therapeutic concentrations, which may further exacerbate toxic side effects and lead to non-specific adverse reactions. Additionally, the rapid excretion of drugs can easily cause peak and trough phenomena, resulting in poor therapeutic effects. In contrast, nanoparticle carriers wrapped in cell membranes have gained widespread application in cancer treatment due to their high biocompatibility. They can disguise themselves as autologous cells, evade recognition and clearance by the immune system, prolong circulation time in the bloodstream, and enhance targeting to tumors. This is crucial for tumor drug delivery and treatment.

Keywords: Nanoparticles, tumor cells, toxic side effects, modified carriers

1. Introduction

This study primarily investigates the side effects and impacts of chemotherapeutic drugs on tumor cells and the human body, focusing on their structural characteristics. The innovative aspect of this study lies in the research on carrier materials for nanoparticles, which can maximize patient compliance, reduce toxicity and side effects, and achieve optimal therapeutic efficacy with the smallest possible dosage. This study mainly explores the application of various types of cell-affinity-modified carriers in namnoparticles.

2. Characteristics of Tumor Cell Proliferation and Differentiation

2.1 DNA and RNA Synthesis

After tumor cells form, their ability to synthesize DNA and RNA significantly increases, while their ability to degrade these components decreases. The increase in nucleic acid components is the material basis for tumor cell growth.

2.2 Protein Metabolism

Tumor cells have strong protein synthesis and deg-

radation capabilities, with a greater capacity for synthesis than degradation. They can even obtain protein degradation products from normal tissues, leading to severe consumption of the human body. This is why many cancer patients, despite eating a lot, are often underweight.

2.3 Enzyme Content

Although the content of oxidase components in malignant tumor cells increases, the content of degradative enzymes rises. Additionally, after the formation of malignant tumors from different sources in human tissues, certain specific functions of the body are lost, leading to almost no difference in the enzyme spectrum within the cells. Specific tissues can no longer perform specific biochemical activities, resulting in systemic damage to the body.

2.4 Glycolysis Process

After tumor cells form, their glycolysis process is enhanced, even under sufficient oxygen conditions. They obtain necessary energy through glycolysis. The metabolic products generated in the glycolysis process can also be utilized by tumor cells to synthesize proteins and nucleic acids, thereby promoting rapid tumor cell growth *[1]* .

3. Nanoparticle-Modified Carriers: Strategies and Mechanisms

3.1 Enhancing Tumor Targeting and Cellular Uptake

The most common treatments currently are chemotherapy and the use of chemical drugs in combination. Chemical drugs themselves are low molecular weight structures that repel high molecular weight biological cells. A common drug like doxorubicin (Doxorubicin) is widely used to treat various types of malignant tumors. It is used to treat leukemia, lymphoma, soft tissue sarcoma, breast cancer, lung cancer, ovarian cancer, multiple myeloma, and other types of tumors. It inhibits tumor growth and spreading by interfering with the survival and proliferation processes of tumor cells. It can also generate reactive oxygen species to disrupt cell permeability. However, long-term use of chemical drugs can lead to significant drug resistance. The endoplasmic reticulum regulates drug resistance in breast cancer cells through subtype-specific pathways (triple-negative breast cancer depends on IRE1α-XBP1, HR + breast cancer depends on PERK). The UPR triggered by it can regulate autophagy-related genes through PERK or IRE1α, and autophagy can feedback regulate its intensity, forming a positive feedback loop. It promotes the formation of autophagosomes but inhibits their degradation, ultimately leading to drug retention and failure in lysosomes *[2]* .

3.2 Overcoming Drug Resistance Mechanisms

Our nanoparticles themselves have a high degree of molecular affinity and can be modified with endoplasmic reticulum components. This makes the endoplasmic reticulum recognize the drug as a component of the body itself, preventing it from activating the three pathway mechanisms and causing the drug to be retained and fail in lysosomes, allowing it to function to the greatest extent possible.

Cholesterol is an important component of human cell membranes. Statins can interfere with cholesterol synthesis pathways, thereby limiting cholesterol synthesis in tumor cells and achieving the purpose of inhibiting proliferation. However, they can also interfere with cholesterol synthesis in normal cells. The nanoparticles we choose can greatly avoid this inhibitory effect on cholesterol synthesis in other cells *[3]* .

3.3 Reducing Systemic Toxicity & Enhancing Selectivity

Firstly, we can modify the surface with nucleic acids. For example, by studying the expression of human heavy chain ferritin (HFtn) in E. coli BL21 (DE3), HFtn was successfully purified by affinity chromatography and size exclusion chromatography. The aptamer AS1411 was chemically modified on the surface of human heavy chain ferritin. Antitumor drugs paclitaxel and photosensitizer ICG were encapsulated into the cavity of aptamer ferritin (HAS1411) by temperature method. The in vitro photothermal performance and in vitro antitumor performance of nanoparticles were evaluated. The study showed that aptamer ferritin had a better cell uptake rate than unmodified ferritin. Under NIR irradiation, HAS1411-PTX-ICG nanoparticles showed the highest cell inhibitory effect *[4]* .

Tumor immunotherapy has attracted widespread attention because it can actively or passively mobilize the body's immune system. However, systemic immunotherapy often causes serious immune-related adverse reactions when stimulating the immune system. Lymph nodes play an important role in antitumor immunity and are the regulatory center of tumor-related immune responses. They provide a suitable microenvironment for the survival, activation, and proliferation of various immune cells. How to deliver drugs more accurately and efficiently to tumor-draining lymph nodes (TDLN) is a major challenge. Nanoparticle-based drug delivery systems (DDS) provide effective lymph node targeting delivery - nanoplates are a class of small-sized disk-shaped particles composed of lipid bilay-

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ers and stabilizing belts. Due to their unique advantages of small size and high biocompatibility, they have gradually been applied to drug delivery research *[5]*.

3.4 Traditional Chinese Medicine - Specific Modification: Application of Ginsenosides

With the rise of traditional Chinese medicine, effective components extracted from natural drugs can also be used to modify the surface of nanoparticles to enhance affinity. Recent studies have found that ginsenosides can not only be used as adjuvants in cancer treatment but also replace cholesterol as carrier materials for liposomes to work synergistically with antitumor drugs in cancer treatment. It has been found that some ginsenoside monomers (such as ginsenoside Rh2) have a steroidal structure similar to cholesterol, which can increase the disorder and hydrogen bond formation of phospholipid fatty acyl chains, thereby promoting the close arrangement of phospholipids and ginsenosides in liposomes and potentially stabilizing the structure of liposomes. In addition, glycosylated ginsenoside monomers significantly affect the properties of liposomes. For example, C-3 glycosylation of ginsenosides can promote the connection between ginsenosides and phospholipids, which is conducive to the long circulation of liposomes in the body. C-3 and C-6 glycosylation can increase the uptake of liposomes by tumor cells, significantly enhancing the tumor targeting of liposomes *[6,7]*.

4. Summary:

Nanoparticles can achieve precise targeted drug delivery due to their similarity to human cell components. They can incorporate cholesterol-like substances to prevent endoplasmic reticulum lysosome degradation and permeability. Their extremely small size helps resist drug resistance and allows them to function specifically in certain cells. This significantly reduces the rate of drug metabolism and toxicity. The surface of nanoparticles can be modified with carriers specific to certain tumor cells, biomimetic components from biological cells, natural active ingredients extracted from traditional Chinese medicine, and specific biological structures to significantly optimize their entry into tumor cells, thereby enhancing the effectiveness and therapeutic index of treatment.

5. Outlook:

With the continuous advancement of human technology and development, various metal-processed and synthetic fiber products are increasingly entering people's lives. These high-molecular synthetic fiber products often have slight toxicity and may potentially trigger the rapid generation of oncogenes within cells, leading to an increase in cancer cases. Current chemotherapy and combined chemical drug therapies often result in issues such as hair loss and poor therapeutic effects. Therefore, we can opt for nanoparticles with higher human affinity, modify their surfaces with chemical components to achieve precise targeted drug delivery, stabilize drug concentration, improve patient compliance, and reduce toxic side effects. Research on chemically modified components holds great promise.

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