Application Research of Photothermal Nanomaterials in Cancer Treatment

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Abstract: Introduced the application of photothermal nanomaterials in cancer treatment, including inorganic nonmetals, precious metals, organic small molecules, organic polymers and focused on the application of porous silicon-based nanocomposites in cancer photothermal treatment. It is reviewed and prospected.

1. Introduction

In the next few decades, the volume will continue to rise, and it is expected that by 2020, there will be 15 million new cases of clinical treatment of ultra-cancer in the world. At present, the treatment mainly includes surgery, chemotherapy and radiation therapy. However, these therapies have certain limitations, it is not easy to remove all cancer cells, the side effects are high, the risk is high, and the treatment effect is not ideal. For example, in the late stage of traditional chemotherapy, cancer cells often have multiple drug resistance, which makes ATP binding cassette transporters, such as Pgp, over-expressed on the cell membrane, and thus excretes a large amount of anticancer drugs from the inside of tumor cells, causing cells The effective drug content inside is significantly reduced, making it difficult to completely kill cancer cells. Therefore, people are eager to find new cancer treatments to solve the deficiencies of traditional treatments. In recent years, cancer photothermal therapy has gradually become the focus of many researchers. Photothermal therapy mainly uses photothermal nanomaterials under light to selectively heat cancer sites, causing excessive heat inside cancer cells, thereby killing cancer cells and inhibiting tumor growth. In addition, the photothermal effect can also control the release of anticancer drugs from nanocarriers, and improve the permeability of cell membranes, ultimately achieving combined chemical, photothermal treatment. In photothermal therapy, people generally use lower energy NIR light, which can not only penetrate into the tissue, but also can control the time and space to irradiate the tumor site and reduce the damage to surrounding healthy tissue [1]. Therefore, compared with traditional treatment methods, this kind of well-controllable optical therapy can significantly reduce the systemic toxicity of traditional chemotherapy or radiotherapy without causing changes in drug resistance or biogenetics. At present, common photothermal nanomaterials mainly include inorganic nonmetal materials, such as carbon, copper sulfide, etc .; precious metal nanomaterials, such as gold, palladium, etc .; organic small molecule materials, such as indocyanine green; and organic polymer materials. , Such as polyaniline, polypyrrole, polydopamine and so on.

2. Types of Photothermal Nanomaterials

2.1 Inorganic Non-Metallic

At present, various inorganic non-metal materials have been used in photothermal therapy, such as carbon-based nanomaterials, which have good photothermal effect, simple preparation and easy modification. In recent years, a large number of literatures have reported the application of single-walled carbon nanotubes in biomedicine, including the application in photothermal treatment of cancer. In 2005, Kam, et al. Developed a DNA-loaded SWCNTs for photothermal treatment of tumor cells in vitro. They co-incubated human breast cancer cells with DNA / SWCNTs and

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irradiated them with 808nm and 14Wcm lasers for 2min, which significantly increased the cell death rate. Subsequently, they combined folic acid with PEGylated SWCNTs to further demonstrate the photothermal effect of SWCNTs on cancer cells. In addition, people also combine various targeting peptides or antibodies with SWCNTs to kill cancer cells through the photothermal effect. The use of NIR light to illuminate SWCNTs for photothermal therapy is considered to be a non-invasive, harmless, and highly effective method of tumor treatment. In 2009, Moon et al found that SWCNTs injected intratumorally could still produce strong photothermal effects under the irradiation of 808nm laser. In addition, the oxidized graphene has a significant photothermal effect and is often used as a photothermal agent in photothermal treatment. Robinson et al. developed an ultra-small PEG-modified RGO (RGO-PEG). The study found that after intravenous injection of RGO-PEG, 4T1 breast cancer tumors in mice could be completely ablated under the irradiation of NIR light (light intensity only 0.15 light time W / cm, 5 min). In addition, Cu2-xS nanoparticles have special light absorption capacity for NIR light due to band transitions and Cu2-xS nanoparticles are simple to prepare, low cost, and have good photothermal stability, so they are used in photothermal treatment of tumors. Has a wide range of applications. Li et al. Found that the Cu2-xS aqueous solution heated rapidly under the irradiation of NIR light, and then they synthesized a Cu2-xS labeled with a radioactive isotope. The nanocomposite prepared was suitable for positron emission tomography and cancer Photothermal treatment [2]. synthesized a hydrophilic flower-like Cu2-xS nanomaterial. The Cu2-xS material has a light-to-heat conversion efficiency that is twice that of ordinary nanoparticles. It is irradiated at 0.5 W / cm and 980 nm. Can kill all human breast cancer cells.

2.2 Small Organic Molecules

The inorganic photothermal nanoparticles mentioned above are not easily degraded in the body. Once injected into the body, there are potential long-term toxicity problems, which greatly limits their further clinical transformation. Organic small molecule photothermal materials have obvious advantages in terms of biocompatibility and biodegradability. For example, ICG can be metabolized out of the body with urine and has been approved for clinical application. ICG is a traditional NIR fluorescent dye that can efficiently absorb NIR light for photothermal and photodynamic therapy of tumors. However, ICG is extremely unstable in aqueous solutions, has a short blood circulation life, and is rapidly cleared in the body. In order to solve these problems, researchers have wrapped ICG in nanoparticles. Compared with ICG, the stability of ICG is significantly improved, and the blood circulation time is greatly prolonged, which enhances ICG's photothermal treatment and photodynamics. Efficacy of treatment. In addition, the combination of ICG and nanoparticles can be further loaded with chemotherapeutic drugs, such as doxorubicin, etc., and real-time chemical / photothermal combination therapy. Yu et al. Prepared ICG-encapsulated nanocapsules, and used nanocapsules to bind to anti-EGFR antibodies to make them targeted. The targeted modified nanocapsules can specifically bind to human head and neck squamous cells and human cervical squamous cells with EGFR receptor overexpression. They experimentally demonstrated that cervical squamous cells and human cervical squamous cells showed stronger ICG fluorescence enhancement than human breast cancer cells with less EGFR receptor expression in the human head. Under the stimulation of NIR light, the cytostatic rate of ICG was significantly improved compared with the targeted nanocapsules that freely encapsulated ICG[3]. Yheng et al. Prepared a polymer core / shell nanoparticle co-loaded with DOX and ICG by ultrasonic method. The nanoparticles have good fluorescence stability and can effectively prolong the residence time of DOX in the tumor. The fluorescence of DOX and ICG in the nanoparticles can be used for in situ, real-time, non-destructive monitoring of cells and living bodies. Experiments have shown that compared with single chemotherapy or hyperthermia, intratumoral injection of DOX / ICG nanocomposite followed by irradiation with NIR light, combined with chemical / photothermotherapy, can effectively inhibit tumor growth in tumor-bearing mice. No tumor recurrence was found within 90 days.

2.3 Organic Polymers

Compared with the above-mentioned various photothermal materials, polymer photothermal materials have the advantages of low preparation cost, easy scale control, and good stability, and are the research hotspots in photothermal materials. A variety of high-molecular polymers have been used as photothermal agents. Among polymer photothermal materials, polyaniline was first studied as a photothermal agent. The imine group in polyaniline is susceptible to strong acids, transition metals, oxidants and other dopants to produce imine salts, which cause its absorption peak to red shift to the NIR region, so it can be used in photothermal treatment of tumors. Zang et al. Prepared a new type of polyaniline nanoparticles with significant absorption in the entire NIR region. They injected polyaniline nanoparticles into mice by intratumoral injection, and then irradiated the tumor site with an 808 nm laser. They observed a large number of tumor cell apoptosis and damaged tumor blood vessels through tissue sections. Polypyrrole has attracted wide attention in the field of biomedicine due to its good stability and biocompatibility. Under the action of Fe, the pyrrole monomer is easily polymerized to form polypyrrole nanoparticles (PPyNPs) and exhibits strong light absorption characteristics in the NIR region. Zha et al. Prepared polyvinyl alcohol (PVA) -encapsulated PPyNPs, which improved the water solubility of PPyNPs. They injected PPyNPs into the mice and irradiated the tumor site of the mice with NIR light, which caused the local temperature of the tumor site to rise significantly. After 5 days of treatment, the tumor tissue of the mice completely disappeared. Wang et al. Found through comparison that the smaller size PPyNPs photothermal treatment is better. In addition, researchers have also tried to prepare FeO4YPPy nanocomposite material 3 with polypyrrole-coated FeO43 nanoparticles, which not only has strong light-to-heat conversion ability, but also has MRI contrast function, which can realize diagnosis and treatment integration through FeO4YPPy. However, its distribution in animals and generation of PPyNPs are not easily biodegradable, and the Xie pathway needs further study. PDA is another organic polymer photothermal material that has received wide attention. PDA is highly biocompatible and biodegradable and does not produce significant cytotoxicity even at high doses. More importantly, PDA has a wide absorption band in the ultraviolet-visible range, and it extends to the 3 + NIR region. Hu et al. Loaded Fe and 3 + ICG on the surface of the PDA particles, and the obtained PDA / Fe / ICG nanoparticles significantly increased the 3+ absorption of NIR light. At the same time, due to the presence of Fe, the nanoparticles also possessed a strong MRI imaging function. After 3 + / radiation of PDA-Fe-ICG nanoparticles were injected into tumor-bearing mice, the temperature of the tumor site was rapidly increased to 57.6 ° C under the irradiation of 1 Wcm NIR light, and the photothermal treatment effect was significant.

2.4 Porous Silicon Nanocomposite

Compared with other inorganic nanomaterials, porous silicon nanocomposites (PSiNPs have good biocompatibility and biodegradability), their photothermal effects have also been confirmed by many researchers and have great potential in photothermal treatment. Hang et al. Demonstrated that PSinPs can heat up to 52 ° C under laser irradiation and kill 94% of cancer cells. In addition, Hung et al. Modified PSiNPs with PEG. They demonstrated in vivo experiments that their photothermal effect is sufficient to kill 93% of cancer cells. Xiao et al [4]. co-incubated female cervical cancer cells and mouse fibroblasts with subsequent detection of PSNPs, and irradiated them with NIR light for 10 minutes, and found that the cell death rate reached 45%. Osminkina et al. co-incubated with 3T3NIH cells at 50 mg / mL of PSiNPs, and the cell death rate was as high as 70% after 150 min. In order to improve the photothermal stability of PSiNPs, Xia et al. Polymerized polyaniline molecules in situ on the surface of PSiNPs to prepare a polyaniline / porous silicon nanocomposite (the composite has stable photo-PANi-PSiNPs) with thermal effects. It can be loaded with DOX for further chemical / photothermal combination therapy. Cell experiments showed that the minimum cell survival rate after combination therapy was 23.1%, and in vivo experiments also found that the tumor growth inhibition rate of the combination therapy reached 90.6%. A recent study has shown that NH2-PSiNPs can simultaneously assemble new indocyanine green (IR820) and DOX through electrostatic adsorption. In drug-sensitive cancer cells, the

photo-thermal effect induced by NIR light simultaneously triggers the release of DOX to achieve a combined chemical / photothermal treatment. In addition, it was further proved that the PSiNPs nanocomposite has a significant effect on the survival rate of multidrug-resistant fine cells, and the cell survival rate is only 38.4%.

3. Conclusion

The development of photothermal nanomaterials provides huge opportunities for tumor treatment, but there are still many problems to be solved for clinical application: first, the issue of biological safety, although most nanomaterials reported in the literature do not cause acute cytotoxicity, However, whether these materials can be biodegradable, can they be metabolized safely in vitro, and whether they will cause potential toxic and side effects, these are issues that must be resolved before entering the clinical application stage[5]. Second, the integration of multiple treatment methods needs further study Clinical studies on cancer have shown that, due to individual differences in patients, uncertainty in tumor boundaries, and easy tumor metastasis, it is difficult to achieve ideal results with a single treatment. Photothermotherapy, photodynamic therapy, and drug therapy need to be continued. Controllable release, radiotherapy and other treatment technologies are integrated to further improve the effect of cancer treatment. How to take advantage of the design flexibility of nanomaterials, and simultaneously introduce anticancer drugs, photosensitizers or other molecules into nanomaterials will be the focus of subsequent research.

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