Proceedings of the 2nd International Conference on Functional Materials and Civil Engineering
DOI: 10.54254/2755-2721/89/20241097

Research Progress on Photothermal Therapy of Malignant Tumor Cells

Jingxuan Li [1,3,*], Shuo Xu[2,4]

[1]Northwestern Polytechnical University, Xi'an, 710072, PR Chin
[2]Xi'An Polytechnic University, Electrical Engineering and Automation, Xi'An, 710600, China
*corresponding author

[3]liliam@mail.nwpu.edu.cn
[4]3186160559@qq.com

Abstract. Malignant tumors, also known as cancer, are among the diseases with the highest incidence and mortality rates in the world. Photothermal therapy (PTT) involves injecting materials with high photothermal conversion efficiency (PTA) into the human body and using the principle of photothermal conversion to kill malignant tumor cells at the lesion site with high temperatures. This paper reviews various methods of photothermal therapy for malignant tumors, summarizes the basic therapeutic logic of photothermal therapy, and forecasts the future development prospects of this treatment method.

Keywords: photothermal therapy, Functional materials, Tumor cell therapy

1. Introduction

Malignant tumors result from the malignant proliferation of normal human cells caused by genetic mutations [1]. These tumors are characterized by uncontrolled growth, metastasis to other organs, and invasion of adjacent organs, leading to the disruption of bodily functions. Both environmental factors and intrinsic factors of the body can contribute to the development of tumors. Current primary treatment methods include surgery, chemotherapy, radiotherapy, targeted therapy, immunotherapy, traditional Chinese medicine, gene therapy, endocrine therapy, hyperthermia, laser therapy, cryotherapy, and others [2]. This paper focuses on the hyperthermia treatment of malignant tumors, discussing methods of treating malignant tumors by applying the theory of photothermal therapy.

2. Principles of Photothermal Therapy for Malignant Tumors

Photothermal therapy (PTT) involves injecting materials with high photothermal conversion efficiency (photothermal agent, PTA) into the human body, where they accumulate near the tumor tissue through directional recognition technology. Under the irradiation of external light sources such as near-infrared (NIR), these materials convert light energy into thermal energy to kill cancer cells [3]. As a non-invasive treatment method, PTT offers advantages such as minimal side effects, high specificity, and the possibility of repeated treatments. Moreover, photothermal therapy not only kills cancer cells but also inhibits the metastasis of tumor cells, characterized by high precision, strong controllability, and low

DOI: 10.54254/2755-2721/89/20241097

side effects. The basic principle involves the absorption of light energy by photosensitizers under near-infrared laser irradiation. The absorbed energy, after undergoing internal conversion and non-radiative transitions like electron vibration relaxation, is released in the form of heat. The resulting high temperature gradually increases the temperature of the tumor tissue. When the temperature reaches 41.5°C, it exerts a toxic effect on tumor cells; when it exceeds 43.5°C, it destroys the blood vessels within the tumor tissue, thus achieving the PTT treatment effect [4].

3. Selection of Photothermal Materials

3.1. Selection Criteria

As carriers for certain drugs, thermal nanomaterials must possess characteristics such as high photothermal conversion efficiency, high surface modification activity, high biocompatibility with biological tissues, high biodegradability, and low toxicity. The structure of nanomaterials determines their optical properties, while the optical absorption spectrum dictates the photothermal conversion efficiency, especially in the near-infrared region. The smaller the size of the thermal nanomaterials, the more it can promote the enhanced permeability and retention (EPR) effect and the targeting modification of tumor cells [5], thereby aiding in the killing of tumor cells during photothermal therapy.

3.2. Material Development

In the progression from organic nanomaterials to inorganic nanomaterials, photothermal nanomaterials have gradually evolved with improved functionality. Each type of material has its own advantages: generally, inorganic photothermal agents (PTA) exhibit higher photothermal conversion efficiency and better photothermal stability compared to organic PTA, while organic PTA is superior in terms of biocompatibility [6].

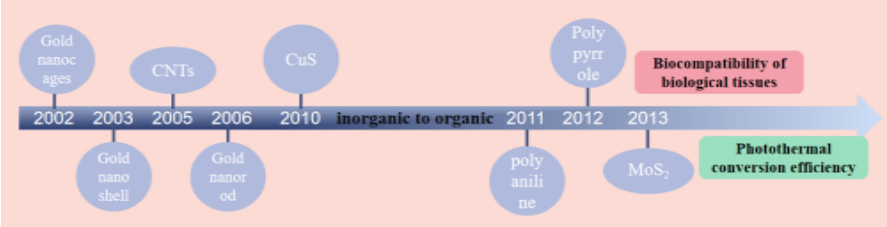

Figure 1. Classification and Development History of Nanophotothermal Converters

3.3. Common PTA Materials

Common organic nanomaterials include: 1) near-infrared dyes, 2) polymeric materials, and 3) other organic PTA materials. Inorganic PTA materials include: 1) gold nanomaterials, 2) metal sulfide nanomaterials, 3) graphene nanomaterials, 4) two-dimensional germanene quantum dots (GeQDs) [7], and 5) other inorganic nanomaterials.

4. Methods of Photothermal Therapy for Malignant Tumors

In the process of tumor photothermal therapy, two main challenges arise: first, the high temperatures can damage normal tissues and organs near the tumor; second, uneven heat distribution may lead to incomplete tumor eradication. To address these issues, the primary design strategies are as follows:

Strategy 1 involves using mild photothermal therapy (MPTT) with relatively lower temperatures (<45°C) to minimize damage to normal tissues. To counteract the reduced therapeutic effectiveness due to lower temperatures, a multimodal synergistic therapy system is constructed to compensate for this shortcoming.

Strategy 2 focuses on targeted therapy methods: with the continuous advancement of nanocarrier drug delivery technology, the maturation of nanoparticle-based drug delivery provides the possibility for precise targeted therapy of tumors. Therefore, using nanomaterials to carry drugs in combination with photothermal therapy enhances the cell-killing effect for precise targeted therapy.

DOI: 10.54254/2755-2721/89/20241097

From these two strategies, it is evident that the key focus of research in photothermal therapy is on the selection of materials—specifically, how to choose materials with good biocompatibility, high photothermal conversion efficiency, and the ability to carry drugs for targeted killing of malignant tumors.

5. Analysis of Research Outcomes in Photothermal Therapy for Malignant Tumors

There are two relevant cases adopting Strategy 1. The first case is the research on mild photothermal therapy (MPTT) led by the Affiliated Hospital of Hangzhou Normal University. This research group combined MPTT with other drugs or therapies to construct a multimodal synergistic treatment system. In this system, the performance of the photothermal agent (PTA) is particularly crucial. Photothermal conversion efficiency (PCE) is a key factor of PTA, as it directly determines the required excitation light intensity during photothermal therapy. High-intensity excitation light can easily damage skin and tissues. Therefore, enhancing the photothermal conversion efficiency of the PTA, reducing laser intensity, and using lasers with safe light intensity for photothermal therapy are challenges in the field of PTA research. Nanoparticle PTAs, which accumulate in tumors through high permeability and retention (EPR effect) and active targeting, have higher photothermal conversion efficiency than small-molecule PTAs and are currently the most widely used and promising photothermal materials in MPTT [8]. Inorganic PTAs offer higher photothermal conversion efficiency and better photothermal stability, while organic PTAs have advantages in biodegradability and biocompatibility. The main types include noble metals, carbon-based materials, and transition metal-based materials, while organic nanomaterials include organic small molecules and polymeric materials.

The second case is the research led by Shaanxi University of Chinese Medicine titled “Application of Photothermal Conversion Nanomaterials in Tumor Photothermal Therapy.” The study identifies several strategies to improve the efficacy of photothermal therapy: 1) increasing the concentration of photothermal agents in tumors, which can be achieved by enhancing both passive targeting and active targeting to accumulate more photothermal agents in tumors; 2) designing and synthesizing novel environment-triggered photothermal agents that only exhibit photothermal conversion capabilities when activated by the tumor microenvironment for precise targeting; 3) compared to the commonly used NIR-I (700-1000nm) window, the NIR-II (1000-1350nm) window has deeper tissue penetration, thus developing new photothermal agents with strong absorption and efficient photothermal conversion in the NIR-II window; 4) optimizing laser parameters can improve the overall therapeutic efficacy of photothermal therapy to some extent; 5) when ablating large solid tumors, the efficacy of a single photothermal therapy may be limited, so a multimodal combined therapy based on photothermal treatment can be used for synergistic treatment [9].

Adopting Strategy 2, Jiangnan University conducted research on “Targeted Nanoparticle Systems for Liver Cancer Treatment Using Photothermal Therapy,” which employs nanobiotechnology to develop a nanoparticle drug delivery system combined with photothermal therapy. The experimental method involves constructing a drug-loaded nanoparticle complex system using graphene oxide as a bio-nanocarrier and verifying the liver cancer targeting capability and tumor inhibition effects of combined chemotherapy and photothermal therapy through in vivo and in vitro experiments [10]. The results indicate that, compared to photothermal therapy or chemotherapy alone, the combined chemophotothermal treatment exhibited significant acute cytotoxic effects, leading to better inhibition of liver cancer cell survival.

6. Conclusion and Outlook

Photothermal therapy (PTT) demonstrates broad application prospects. High temperatures can disrupt the blood vessels within tumor tissues, effectively inhibiting tumor growth. However, there are still many challenges to address in clinical applications, such as uneven heat distribution, incomplete tumor eradication, and the potential for significant damage to healthy tissues [11]. Additionally, tumor cells currently exhibit varying degrees of resistance to photothermal effects, leading to ineffective tumor ablation. This resistance primarily stems from the cellular mechanism of “autophagy” [12]. Cell damage

DOI: 10.54254/2755-2721/89/20241097

induced by heating can be repaired and reversed through the autophagy process, resulting in incomplete cell necrosis. Moreover, most current photothermal therapies employ low-temperature treatments. Although treatment temperatures need to exceed 50°C to effectively kill tumor tissues, excessively high temperatures can cause severe skin burns, triggering a series of self-defense responses (such as the release of inflammatory factors) in the body. These defense responses may further increase the risk of tumor metastasis and recurrence.

In summary, to achieve optimal therapeutic outcomes, photothermal therapy should be combined with other treatment modalities, such as chemotherapy, gene therapy, and immunotherapy. This approach can not only achieve effective treatment of malignant tumors but also leverage the inherent advantages of photothermal therapy. For example, several studies have shown that the combination of mild photothermal therapy with chemotherapy can effectively address chemotherapy drug resistance and enhance the efficacy of tumor treatment [13]. Overall, photothermal therapy for malignant tumors holds significant research potential.

References

[1] Bray, F., Ferlay, J., Soerjomataram, I., et al. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 68, 394–424.

[2] Xue, K. H., Wei, F., Lin, J. Y., et al. (2021). Tumor acidity-responsive carrier-free nanodrugs based on targeting activation via ICG templated assembly for chemotherapy. Biomaterials Science, 9(3), 1008-1019.

[3] Beik, J., Abed, Z., Ghoreishi, F. S., et al. (2016). Nanotechnology in hyperthermia cancer therapy: From fundamental principles to advanced applications. Journal of Controlled Release, 235, 205–221.

[4] Chen, W. H., Luo, G. F., Lei, Q., et al. (2017). Overcoming the heat endurance of tumor cells by interfering with the anaerobic glycolysis metabolism for improved photothermal therapy. ACS Nano, 11, 1419–1431.

[5] Huang, L., Li, Y., Du, Y., et al. (2019). Mild photothermal therapy potentiates anti-PD-L1 treatment for immunologically cold tumors via an all-in-one and all-in-control strategy. Nature Communications, 10, 4871.

[6] Wang, Y., Huang, Q., He, X., et al. (2018). Multifunctional melanin-like nanoparticles for bone-targeted chemo-photothermal therapy of malignant bone tumors and osteolysis. Biomaterials, 183, 10–19.

[7] Ding, F., Gao, X., Huang, X., et al. (2020). Polydopamine-coated nucleic acid nanogel for siRNA-mediated low-temperature photothermal therapy. Biomaterials, 245, 119976.

[8] Zhou, Z., He, H., Wang, K., et al. (2020). Granzyme A from cytotoxic lymphocytes cleaves GSDMB to trigger pyroptosis in target cells. Science, 368(6494), eaaz7548.

[9] Zhang, Z., Zhang, Y., Xia, S., et al. (2020). Gasdermin E suppresses tumor growth by activating anti-tumor immunity. Nature, 579(7799), 415–420.

[10] Gai, S., Yang, G., Yang, P., et al. (2018). Recent advances in functional nanomaterials for light-triggered cancer therapy. Nano Today, 19, 146–187.

[11] Yoon, H. J., Lee, H. S., Jung, J. H., et al. (2018). Photothermally amplified therapeutic liposomes for effective combination treatment of cancer. ACS Applied Materials & Interfaces, 10(7), 6118–6123.

[12] Ashrafizadeh, M., Mohammadinejad, R., Tavakol, S., et al. (2021). New insight into triple-negative breast cancer therapy: The potential roles of endoplasmic reticulum stress and autophagy mechanisms. Anticancer Agents in Medicinal Chemistry, 21(6), 679–691.

[13] Guo, X. L., Li, D., Sun, K., et al. (2013). Inhibition of autophagy enhances anticancer effects of bevacizumab in hepatocarcinoma. Journal of Molecular Medicine, 91(4), 473–483.