Review

Antitumor Applications of Photothermal Agents and Photothermal Synergistic Therapies

Chaowei Li 1,†, Yue Cheng 1,2,†, Dawei Li 1,2,* , Qi An 1,2, Wei Zhang 1,2, Yu Zhang 1,2 and Yijun Fu 1,2,*

1 School of Textile and Clothing, Nantong University, Nantong 226019, China; 13063589580@163.com (C.L.); cy970218@126.com (Y.C.); anqi960110@163.com (Q.A.); zhangwei@ntu.edu.cn (W.Z.); z.yu@ntu.edu.cn (Y.Z.)
2 National & Local Joint Engineering Research Center of Technical Fiber Composites for Safety and Health, Nantong University, Nantong 226019, China
* Correspondence: ldwntu@163.com (D.L.); fuyj@ntu.edu.cn (Y.F.)
† These authors contributed equally to this work.

Abstract: As a new tumor treatment strategy, photothermal therapy (PTT) has the advantages of accuracy, ease of administration, a high efficiency and low side effects. Photothermal transduction agents (PTAs) are the key factor which play an important role in PTT. The mechanism of PTT is discussed in detail. The photothermal conversion efficiency (PCE) can be improved by increasing the light absorption and reducing the light scattering of photothermal conversion agents. Additionally, non-radiative relaxation path attenuation can also promote energy conversion to obtain a higher value in terms of PCE. The structure and photothermal characteristics of various kinds of PTAs (metal materials, carbon-based nanomaterials, two-dimensional nanomaterials, and organic materials) were compared and analyzed. This paper reviews the antitumor applications of photothermal synergistic therapies, including PTT combined with immunotherapy, chemotherapy, and photodynamic therapy. This review proposes that these PTAs promote the development of photothermal synergistic therapies and have a great potential in the application of tumor treatment.

Keywords: photothermal therapy; photothermal transduction agents; nanoparticles; antitumor

1. Introduction

According to a recent World Health Organization report on cancer, one out of every six people dies from the disease. Surgery, chemotherapy, radiation, immunotherapy, targeted therapy, and other treatments are currently used to treat cancer [1,2]. Surgical treatment has played an essential role in removing malignancies from the body since the invention of anesthesia in 1846, especially when paired with chemotherapy and imaging technology. Surgical treatment, however, is still ineffective due to the difficulty of removing microscopic tumor cells that are simple to disseminate and promote tumor recurrence [3,4]. Chemotherapy is frequently used in conjunction with one or more than one other medication to kill cancer cells [5], and the drugs can circulate to most tissues and organs throughout the body for systemic treatment [6]. However, chemotherapy has some defects, for example, the growth of drug resistance, the nonspecific systemic dispersion of antineoplastic agents, low concentrations of medications reaching the target, and large toxic side effects, which have all contributed to major treatment consequences, such as hindering the proliferation of normal cells and damaging human tissues and organs [7,8].

Radiation therapy is one of the main modalities of clinical oncology, which destroys cancer cells by generating localized ionizing radiation to achieve anti-tumor effects [9]. This treatment is critical for patients whose tumors are inoperable or incompletely removed as well as those with recurrent disease [10]. In some cases, radiotherapy can treat tumors by inducing immunogenic cell death to induce systemic immunotherapy effects [11,12], and local irradiation has also been reported to eradicate treated tumors [9]. Unfortunately, radiation therapy can cause radiation damage to adjacent normal tissue, resulting in scar
tissue that leads to systemic immunosuppression. In addition, the inherent resistance of tumors to radiotherapy, the lack of oxygen in the tumor microenvironment, and strong systemic and local toxic side effects greatly limit the efficacy of cancer radiotherapy \[13,14\]. As a result, novel tumor therapy strategies with less damage to normal cells and better therapeutic impacts are required.

Immunotherapy, gene therapy, photodynamic therapy (PDT), and photothermal therapy (PTT) are examples of new cancer treatments that have considerably enhanced the effectiveness of tumor treatment \[15–19\]. Due to its advantages of a low cost, high efficiency, minimal invasiveness, few side effects, and strong targeting, photothermal treatment has garnered a large amount of interest in tumor therapy \[20–23\]. Photothermal transduction agents (PTAs) are used in PTT to convert light energy into heat energy. PTAs are injected into the body, and, using targeting technology, they accumulate near tumor tissue, where they damage the protein structure of tumor cells, resulting in a cure. PTT has the advantage of being able to use variable levels of external laser irradiation to precisely target the tumor while avoiding harm to the surrounding healthy tissue; it can also be used to treat all types of cancer and is non-invasive \[24–26\].

The major issue with PTT at this juncture is its low depth of light penetration, which can result in the inadequate ablation of malignancies outside of the irradiation area. Furthermore, the delivery PTAs in tumors is inefficient, the overheating of tumor areas leads to unnecessary damage to normal tissues, and there is chance of the development of drug resistance. The mechanism of PTT was investigated in this work, and many forms of PTAs were introduced. The use of PTT in combination with immunotherapy, chemotherapy, and PDT in tumor treatment was investigated, and the prospects of applying PTT are presented.

2. Mechanism of PTT

Studies have shown that the biochemical reaction rate of cells increases significantly with an increase in temperature, which is due to the increase in reactive oxygen species, the density in cells, oxidative stress, and oxidative damage to nucleic acids, lipids, and proteins \[27\]. In the near infrared (NIR) window (650–1000 nm), low light absorption and the transparency of healthy tissues allow for deep penetration into the body. PTT uses the strong light absorption and high photothermal conversion efficiency (PCE) of PTAs to absorb light energy and effectively convert it into heat energy, so as to increase the temperature of local tumors, which leads to the cell membrane rupture or protein degeneration of tumor cells, and avoid damage to normal cells \[28–30\]. Studies have found that factors such as tumor type, NIR light irradiation conditions, and the heat absorbed by cells all have a specific impact on PTT-induced cell death \[31\]. The main mechanism behind PTT involves a local high temperature inducing various changes in tumor cells. For example, PTT-induced hyperthermia triggers the release of antigens, pro-inflammatory cytokines, and immunogenic intracellular substrates from dying tumor cells, thereby promoting the activation of antitumor immunity \[32\]. Furthermore, PTT generates excess reactive oxygen species (ROS) under NIR irradiation, including hydroxyl radicals, hydrogen peroxide superoxide, and singlet oxygen \[33\]. Excessive ROS leads to the destruction of DNA, proteins, and lipids, eventually causing the apoptosis of cancer cells, which is considered to be another anticancer mechanism of PTT \[34\]. Prasad et al. reported that carbon dots can convert NIR light into heat and generate ROS, leading to 4T1 cell death and breast tumor ablation \[35\].

When irradiated by NIR light, PTAs can both absorb and scatter light. The sum of the two is called extinction. Only the absorbed energy can be partially converted into heat, and the absorption, scattering, and extinction coefficients of PTAs are related to the size, shape, and composition of PTA nanoparticles \[25,36\]. When photons radiated by NIR collide with small molecule chromophores, electrons are excited from their ground state \(S_0\) to a higher singlet state \(S_1\). They are then relaxed to the lowest excited state through internal conversion \[37\]. The relaxed molecules at the lowest vibrational level of the excited state can undergo one of the following three processes: (1) they can return to the ground state by emitting
Metal materials with high oxidation resistance are the most studied inorganic PTAs, with these including Au, Ag, Pt, and Pd [60]. They can absorb laser to excite electrons from the ground state to the excited state, and they can then release energy in the form of heat through nonradiative decay. Because precious metal materials have the advantages of easy surface modification and good biological stability, these factors can improve the PCE [61]. Currently, the gold nanostructures studied include gold nanorods [62], gold nanoshells [63], gold cages, gold nanorings [64], gold nanoparticles [65], rice vesicles, and chiral gold nanoparticles [66]. Since PTT containing gold nanoparticles was first reported in 2003, the research on gold nanomaterials has attracted extensive attention [67].
Nishikawa et al. [68] prepared an injectable anti-shear hydrogel composed of gold nanorods and nanospheres linked by CpG oligonucleotides. NIR irradiation hydrogel can stimulate heat shock protein 70 and mRNA expression, while reducing the volume of primary tumors. Gold nanomaterials have also been proved to have strong photothermal efficiency and can be used in combination with immunotherapy. In addition, Liu et al. [69] proposed gold-shell silica nanoparticles, and Mohammad et al. [70] proposed gold-shell Fe₃O₄ nanoparticles. Due to the hollow nanostructure of gold nanoshells, these materials show high light absorption in the NIR band.

Although metal materials provide an excellent photothermal effect for cancer treatment, there remain a number of problems which need to be solved: (1) gold nanomaterials are not biodegradable, so it is necessary to further detect the treated gold nanomaterials, and (2) gold nanomaterials have poor optical stability. Under continuous NIR irradiation, some specific gold nanomaterials are deformed due to the “melting effect” [71], and the photothermal effect is reduced. Therefore, precious metal materials need to be studied further.

3.2. Carbon Based Nanomaterials

Carbon based nanomaterials, including carbon nanotubes and graphene, have attracted much attention due to their excellent photothermal properties and biocompatibility in the medical field [72]. Among them, carbon nanotubes can effectively combine chemotherapy with PTT to enhance the anti-tumor effect. As carbon nanotubes have high a specific surface area and high PCE, they can be used as potential carriers for the transport of nucleic acids, proteins, and drug molecules in cells. They are therefore being employed in the development of the next generation of PTAs [73,74].

In order to further improve the PCE, multi-walled carbon nanotubes (MWCNT) have been developed. These consist of a nested columnar structure with diameters ranging from several nanometers to several microns. Compared with single-walled carbon nanotubes (SWNT), they can load more drugs and absorb more NIR radiation, making them an ideal medium for chemical–thermal combination therapy [75–77].

Zhou et al. [78] developed SWNT-based thermosensitive hydrogels for the treatment of xenograft gastric cancer mice, as shown in Figure 2. First, injectable hydrogels can deliver the anticancer drug doxorubicin hydrochloride (DOX) directly to the tumor site, enabling it to play an anticancer role in situ. At the same time, NIR light can provide hyperthermia by penetrating tissue to stimulate SWNT located at the tumor site. The DOX released by the drug loading system exceeded 20% on the first day of injection, and the cumulative release reached approximately 96% on the 28th day, indicating that SWNT-GEL had the function of sustained drug release. In addition, after the intratumoral injection of SWNT, the tumor growth rate of mice was 156% with NIR and 261% without NIR after 28 days of treatment, respectively. The disease of the mice continued to be in remission under NIR irradiation.

3.3. Two-Dimensional Nanomaterials

2D nanomaterials have the advantages of an ultra-thin atomic thickness, a low toxicity, a controllable size, and a large specific surface area. They have unique physical and chemical properties, an easy surface modification, a high photothermal efficiency, and can promote the extension of tumor blood circulation and improve the accumulation capacity. 2D nanomaterials mainly include graphene and its derivatives, metal compounds [79,80], transition metal dihydroxy compounds (TMDC) [81], black phosphorus (BP) [82,83], and transition metal carbides/carbonitrides (MXene) (e.g., carbides, nitrides, or carbonitrides) [84–86].

3.3.1. Transition Metal Dihydroxy Compounds

TMDCs include MoS₂, WS₂, TiS₂, and MoSe₂, which have high PCE, a good biocompatibility, and photothermal stability [87]. A TMDC is basically a layer of transition metal atoms (such as Ti, Zr, Hf, V, Nb, Ta, Mo, and W) sandwiched between two layers of sulfur atoms (such as S, Se, and Te). In particular, molybdenum disulfide (MoS₂) shows good absorption characteristics in the NIR spectrum range, the element Mo widely exists in
the identifiable elements of some enzymes, and the content of S in the body is rich, so MoS$_2$ is biocompatible. In 2013, it was first proved that MoS$_2$ nanoparticles were a new PTT material similar to graphene oxide (GO). Compared with gold nanorods, they have greater capacity for NIR absorption. However, MoS$_2$ and higher PCE (62.5%) materials disperse poorly in aqueous solution and cannot locate specific tissue sites, which limits their application in targeting cancer nanodrugs. Therefore, MoS$_2$ is often used in PTT and other combination therapies [88].

Figure 2. (A) The xenograft tumor model was established by subcutaneous injection of BGC-823 gastric cancer cells in mice. DOX/SWNT-GEL was injected into the tumor, and then the mice received NIR laser irradiation at the tumor site; (B) DOX release curve of SWNT-GEL in PBS for 28 days at a constant temperature of 43 °C; (C) tumor growth rate of mice treated with different methods and NIR radiation; (D) tumor growth rate of mice with different treatments without NIR radiation. Data was presented as mean ± SD (* indicates $p < 0.05$ and ** denotes $p \leq 0.01$, compared with DOX/SWNT-GEL/NIR or DOX/SWNT-GEL group). Reproduced with permission from ref. [78] Copyright (2015). Wiley-VCH Verlag.

Because GO is highly soluble in aqueous solution, it exhibits obvious targeting, a high absorption, and an excellent PCE in the NIR range. Liu et al. [89] doped GO monolayers onto an MoS$_2$ layer to prepare MoS$_2$/GO nanocomposites. Figure 3 shows the schematic diagram of its structure and therapeutic mechanism. The PCE was as high as 42% when photoacoustic imaging and PTT were performed simultaneously in live mice. Tissue targeting studies have shown that MoS$_2$/GO composite material preferentially accumulates in the lung, indicating
that MoS$_2$/GO composite material targets the lungs, indicating a direction for the treatment of emphysema diseases such as chronic bronchitis and bronchial asthma.

**Figure 3.** MoS$_2$/GO nanocomposites. (A) The overall schematic diagram depicting functionality and biocompatibility enhancement through the synthesizing of MoS$_2$/GO nanocomposites; (B) in vivo biodistribution of various materials in mice. The Mo contents were examined in mice 24 h post i.v. injection. The results from ICP-MS determination were shown as % of injected. In vivo imaging and lung accumulation analysis; (C) ICG fluorescent images of lungs from mice 24 h post-injection of free ICG and ICG-loaded nanomaterials; (D) quantification of relative ICG fluorescence in lungs ($n = 3$). ICG, indocyanine green. DOX loading capacity and tumor killing efficacy of different materials; (E) DOX loading capacity of nanomaterials ($n = 4$). * indicates $p < 0.05$ and # denotes $p < 0.001$, compared to bulk MoS$_2$-treated group; (F) in vitro tumor killing efficacy of DOX-loaded materials at the same mass concentrations ($n = 5$). The concentrations of materials were tailored for each type of cells as follows: 2 $\mu$g·mL$^{-1}$ for LLC cells, 6 $\mu$g·mL$^{-1}$ for B16 cells, 30 $\mu$g·mL$^{-1}$ for 4T1 cells, and 15 $\mu$g·mL$^{-1}$ for MDA-MB-231 cells; (G) representative images of metastatic tumor nodules in the lungs from treated and untreated mice with implantation of B16 murine melanoma cancer cells. DOX, doxorubicin; LLC, Lewis lung carcinoma. Reproduced with permission from ref. [89]. Copyright (2018). Springer Nature.

**3.3.2. Transition Metal Carbides/Carbonitrides**

MXene has an energy band structure similar to that of semi-metal, that is, a local surface plasmon resonance effect similar to that of metal nanoparticles [90,91]. It exhibits an excellent electromagnetic wave absorption performance and dissipates the absorbed wave in the form of heat inside the substance. It is a new 2D material with a wide range of applications. MXenes used for photothermal effect include titanium carbide, niobium carbide, and tantalum carbide [92,93]. The most commonly used are titanium carbide nanoparticles.

Li et al. [94] used a Ti$_3$AlC$_2$ ternary-layered carbonitride (MAX) phase as a raw material and etched an Al layer with hydrofluoric acid (HF) aqueous solution. Under the action of ultrasound, the pretreated HF-treated MAX phase was immersed in DMSO to form a peeling single layer or a small amount of layered MXene flakes. The absorption peak of MXene is about 800 nm, while CNT absorbs a wide spectrum of 300–1300 nm, but there is no obvious absorption peak, so it can be seen that MXene has a higher light absorption capacity than CNT. In addition, no matter if the wavelength of the laser source is 473 nm
or 785 nm, the PCE of MXene is close to 100%, which indicates that MXene is an excellent photothermal material.

3.3.3. Black Phosphorus

Since 2015, BP nanomaterials have attracted significant attention in the biomedical field because of their high PCEs, large specific surface areas, good biocompatibility, and biodegradability. As metal-free layered semiconductor materials, BP nanomaterials have a thick-dependent band gap and can be tuned from 0.3 eV in volume to 2.0 eV as a single layer. BP usually exists in the form of nanoparticles, quantum dots, and nanosheets [95]. Compared with 2D materials such as graphene and MoS$_2$, BP has a higher surface volume ratio due to its folded lattice structure, which can improve drug loading. BP is also photostable, biocompatible, biodegradable [96], and can be easily combined with other cancer treatments due to its absorbance across the entire NIR range.

Yang et al. [97] modified BP nanosheets with polyethylene glycol (PEG) and loaded with chlorin (Ce6) photosensitizer to obtain BP@PEG/Ce6 NSs (as shown in Figure 4). After injection into mice, BP@PEG/Ce6 NSs was transmitted to cervical cancer cells through an enhanced permeability and retention effect, showing good tumor targeting. In vitro experiments have shown that BP@PEG/Ce6 NSs can effectively produce photoheat and reactive oxygen species by releasing Ce6 photosensitizers, thus increasing cell membrane permeability and drug uptake. The related PCE is 43.6% under the NIR light at 660 nm. This material has potentially broad applications in the treatment of PTT.

![Figure 4](image_url)

**Figure 4.** (A) Schematic representation of BP@PEG/Ce6 NSs preparation and its application as fluorescence and thermal imaging guided photothermal and photodynamic cancer therapy; (B) fluorescence images of HeLa cells cultured with BP@PEG/Ce6 NSs; (C) intracellular ROS generation of HeLa cells treated with BP@PEG/Ce6 NSs and irradiated with 660 nm laser. Relative viabilities of HeLa cells after being treated with BP@PEG NSs, Ce6, and BP@PEG/Ce6 NSs at different concentrations of BP@PEG NSs (1, 2.5, 5, 10, 25, and 50 ppm) or Ce6 (0.13, 0.325, 0.65, 1.3, 3.25, and 6.5 ppm); (D) without and (E) with irradiation (660 nm, 0.65 W·cm$^{-2}$, 10 min); (F) fluorescence images of HeLa cells co-stained with Calcein AM (live cells, green) and PI (dead cells, red) upon the addition of BP@PEG NSs, Ce6, and BP@PEG/Ce6 NSs without and with irradiation (660 nm, 0.65 W·cm$^{-2}$, 10 min). Reproduced with permission from ref. [97]. Copyright (2018). American Chemical Society.
In addition, some metal compounds with biocompatibility, such as oxides, sulfides [98], and selenides, etc., can also be used as PTAs in cancer therapy due to their plasmon resonance properties [99,100].

3.4. Organic Materials

So far, organic PTAs based on NIR response small molecules (anthocyanin, porphyrin [101], phthalocyanine [102], and theobromine [103]) and semiconductor polymer nanoparticles (polyaniline [104] and polypyrrole [105]) have shown excellent therapeutic efficacy and have been widely studied as potential PTAs.

PTAs based on small organic molecules, such as cyanine dyes and porphyrins, are often used in cancer imaging and treatment. However, they have poor water solubility, limited tumor accumulation, and low photobleaching and photothermal efficiency. In order to solve this problem, organic nanocarriers can be wrapped to improve solubility and pharmacokinetics, enhance tumor penetration and retention in vivo, and improve photobleaching and photothermal efficiency [5]. So far, organic nanocarriers such as polymer micelles, vesicles, and liposomes have been widely used in photothermal cancer treatment.

As a photothermal conversion agent, IR825 dye has a high absorption coefficient and low fluorescence quantum yield. However, due to its extremely low water solubility and minimal absorption efficiency, therapeutic applications are greatly limited. By using nanocarriers, Li et al. [106] incorporated IR825 into heat-responsive liposomes to enhance bioavailability and photothermal effects in vivo, as shown in Figure 5. The results show that the material retains the high PCE and high photothermal properties of IR825. In vitro and in vivo experiments confirmed that DOX-loaded IR825 mixed with thermoresponsive liposomes combined with PTT can achieve a better tumor suppressive effect than liposomes, DOX, or photothermal ablation alone.

![Figure 5](image-url)
4. Photothermal Synergistic Therapies

As PTT penetrates into tissues, the power of light may decrease, and the uneven heat distribution and severe hypoxia in tumor tissues in PTT make it difficult to eradicate tumors in a single mode of treatment. Therefore, collaborative therapy is an effective way to solve these problems [107]. First, synergistic therapy helps to reduce side effects because the dose of each therapy can be reduced while the overall therapeutic effect can be maintained. Second, interactions between different treatments can produce greater efficiency. For example, heat generated by the photothermal effect can improve the efficacy of some anticancer drugs [108,109].

NIR light (wavelength 650–900 nm) has the characteristics of weaker tissue absorption and larger tissue penetration depth, which is more suitable for PTT [32]. NIR-induced heat production can not only lead to the damage of malignant cells, but also enhance the efficacy of other treatment modalities, thus enabling photothermal synergistic therapy. Photothermal synergistic therapy can be achieved through different working mechanisms such as the photothermal-controlled release of therapeutic drugs, photothermal-enhanced enzyme activity, photothermal-regulated gene expression, photothermal-triggered immune response activation, and photothermal-enhanced chemical reactions [110].

4.1. PTT and Immunotherapy Synergistic Therapy

Immunotherapy is an effective method for cancer treatment. It destroys cancer cells by activating the human immune system on the basis of tumor immunology [111]. The combination of PTT and immunotherapy can achieve an synergistic antitumor effect. On the one hand, PTT-induced cancer cell death can release a tumor specific antigen in situ and trigger a specific anti-tumor immune response. On the other hand, patients can eliminate diffuse metastases beyond the scope of the laser irradiation range and prevent tumor recurrence by relying on their own immune function [112,113].

Wang et al. [114] reported that thermal ablation-induced immune responses based on SWNT could not fully inhibit the growth of secondary tumors. Anti-CTLA4 antibody was introduced after the thermal ablation of the primary tumor, which greatly improved the efficacy and directed the immune checkpoint pathway of abnormal immune response to PD-L1 and IDO.

Chen et al. [115] introduced the in situ autologous tumor vaccine for the combined treatment of PTT and immune adjuvant GC targeting primary tumors. The advantage of the vaccine is the ability to treat different tumors as antigens derived from the tumor itself, so that any subtle differences in the antigen spectrum are captured accordingly.

4.2. PTT and Chemotherapy Synergistic Therapy

While killing cancer cells, chemotherapy drugs may also cause collateral damage to normal cells through oxidative stress [116]. Due to the synergistic effect of PTT and chemotherapy, the ability of tumor metastasis can be controlled to achieve targeted therapy and reduce damage to normal tissues [117]. Currently, much research is focused on developing nanosystems for drug delivery.

Chen et al. [118] coated amorphous carbon on a mesoporous silica carrier on a rGO sheet and constructed a new photoresponsive drug carrier with a photothermal effect and nanometer biscuit structure, which can release drugs and generate a large amount of heat under NIR irradiation (as shown in Figure 6). With good biocompatibility and an efficient cell uptake, the material successfully cleared subcutaneous tumors within 14 days after 5 min of NIR irradiation without distal damage. It is an excellent new delivery platform for combined chemotherapy/hyperthermia.
Photothermal synergistic therapy can be achieved through different working mechanisms such as the photothermal-controlled release of therapeutic drugs, photothermal-enhanced chemical reactions, enzyme activity, photothermal-regulated gene expression, photothermal-triggered immunological reaction, and photothermal-enhanced immunotherapy. These coupled treatment options offer prospective options for future research and development.

4.3. PTT and Photodynamic Synergistic Therapy

Compared with traditional therapies, PDT uses light source targeting to selectively eliminate primary and recurrent tumors, thus avoiding normal tissue damage, narrowing surgical scope, improving patient safety, activating immune function, and reducing recurrence [120]. PDT is made up of three basic components: light, PS, and oxygen. PDT involves mixing a photosensitizer into the target and then illuminating it with light at a wavelength corresponding to the photosensitizer’s absorption band [121]. After irradiation, type I and type II REDOX reactions will occur, leading to the generation of singlet oxygen and other superoxide ions. Finally, these singlet oxygen and superoxide ions can act as target killers [122,123]. PTT and PDT are two major non-invasive medical technologies in the treatment of cancer and other diseases [124]. The combined application of PTT and PDT can not only stimulate the efficiency of the photothermal enhancement of PDT, but also induce the synergistic effect, which can accelerate the flow of blood in the tumor and lead to more oxygen entering the tumor, thus enhancing the efficiency of PDT.

In order to compare the efficacy of porous PDT and PTT in hyperoxic and hypoxic tumors, Taratula et al. [125] studied, for the first time, the nanostructure-driven transformation of porphyrin PDT activation mechanism in an in vivo hypoxic tumor model. In addition, he also designed the application of boron platinate-dipyrrrolidone and silicon-naphthalocyanine in phototherapy against tumors.

5. Conclusions and Outlooks

PTT is a novel approach to tumor treatment, and the advancement of PTAs in the production and use of PTT technology has aided its advancement. Taking advantage of the flexibility afforded in the design of nanomaterials, anticancer drugs, targeted carriers, or...
other therapeutic molecules could be incorporated into PTAs to achieve a combination of PTT, chemotherapy, PDT, immunotherapy, and other cancer treatment methods, thereby improving the therapeutic effect. Because the small penetration depth of light is the most significant barrier to PTT, the development relevant medical devices, such as ultra-micro fiber, is required, so that laser may be converted to deep tissue and play a therapeutic role. On the other hand, photothermal therapy agents must be delivered to tumor sites and the effects of PTT must be monitored using appropriate tools such as MRI and ultrasound.

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**References**

1. Shao, R.; Wang, Y.; Li, L.; Dong, Y.; Zhao, J.; Liang, W. Bone tumors effective therapy through functionalized hydrogels: Current developments and future expectations. *Drug Deliv.* 2022, 29, 1631–1647. [CrossRef] [PubMed]
2. Lau, K.H.; Tan, A.M.; Shi, Y. New and Emerging Targeted Therapies for Advanced Breast Cancer. *Int. J. Mol. Sci.* 2022, 23, 2288.  [PubMed]
3. Wang, P.; Sun, S.; Ma, H.; Sun, S.; Zhao, D.; Wang, S.; Liang, X. Treating tumors with minimally invasive therapy: A review. *Mater. Sci. Eng. C Mater. Biol. Appl.* 2020, 108, 110198. [CrossRef] [PubMed]
4. Alberro, J.A.; Ballester, B.; Deulofeu, P.; Fabregas, R.; Fraile, M.; Gubern, J.M.; Janer, J.; Moral, A.; de Pablo, J.L.; Penalva, G.; et al. Effects of radiation on metastasis and tumor cell migration. *Chem. Lett.* 2022, 41, 4169–4174. [CrossRef] [PubMed]
5. Zhang, W.; Zhang, J.; Liu, T.; Xing, J.; Zhang, H.; Wang, D.; Tang, D. Bidirectional effects of intestinal microbiota and antibiotics: A new strategy for colorectal cancer treatment and prevention. *J. Cancer Res. Clin. Oncol.* 2022. [CrossRef] [PubMed]
17. Xu, J.J.; Zhang, W.C.; Guo, Y.W.; Chen, X.Y.; Zhang, Y.N. Metal nanoparticles as a promising technology in targeted cancer treatment. Drug Deliv. 2022, 29, 664–678. [CrossRef]

18. Fatima, H.; Jin, Z.Y.; Shao, Z.; Chen, X. Recent advances in ZnO-based photosensitzers: Synthesis, modification, and applications in photodynamic cancer therapy. J. Colloid Interface Sci. 2022, 621, 440–463. [CrossRef]

19. Guo, B.; Huang, Z.; Shi, Q.; Middha, E.; Liu, B. Organic Small Molecule Based Photothermal Agents with Molecular Rotors for Malignant Breast Cancer Therapy. Adv. Funct. Mater. 2020, 30, 1907093. [CrossRef]

20. Liu, S.; Fan, X.; Liu, H. Two-Dimensional Nanomaterials for Photothermal Therapy. Angew. Chem. Int. Ed. Engl. 2020, 59, 5890–5900. [CrossRef]

21. Sun, W.; Zhao, X.; Fan, J.; Du, J.; Peng, X. Boron Dipyrromethene Nano-Photosensitizers for Anticancer Phototherapies. Small 2019, 15, 1804927. [CrossRef] [PubMed]

22. Ng, C.W.; Li, J.; Pu, K. Recent Progresses in Phototherapy-Synergized Cancer Immunotherapy. Adv. Funct. Mater. 2018, 28, 1804688. [CrossRef]

23. Curran, W.J., Jr.; Paulus, R.; Langer, C.J.; Komaki, R.; Lee, J.S.; Hauser, S.; Movsas, B.; Wasserman, T.; Rosenthal, S.A.; Gore, E.; et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: Randomized phase III trial RTOG 9410. J. Natl. Cancer Inst. 2011, 103, 1452–1460. [CrossRef]

24. Li, X.; Yong, T.; Wei, Z.; Bie, N.; Zhang, X.; Zhan, G.; Li, J.; Qin, J.; Yu, J.; Zhang, B.; et al. Reversing insufficient photothermal therapy-induced tumor relapse and metastasis by regulating cancer-associated fibroblasts. Nat. Commun. 2022, 13, 2794. [CrossRef]

25. Li, Y.; Bhattacharai, P.; Dai, Z.; Chen, X. Photothermal therapy and photoacoustic imaging via nanotheranostics in fighting cancer. Chem. Soc. Rev. 2019, 48, 2053–2108. [CrossRef]

26. Gao, D.; Zhang, B.; Liu, Y.; Hu, D.; Sheng, Z.; Zhang, X.; Yuan, Z. Molecular Engineering of Near-Infrared Light-Responsive BODIPY-Based Nanoparticles with Enhanced Photothermal and Photoacoustic Efficiencies for Cancer Theranostics. Theranostics 2019, 9, 5315–5331. [CrossRef]

27. Jaque, D.; Martinez Maestro, L.; del Rosal, B.; Haro-Gonzalez, P.; Benayas, A.; Plaza, J.L.; Martin Rodriguez, E.; Garcia Solé, J. Nanoparticles for photothermal therapies. Nanoscale 2014, 6, 9494–9530. [CrossRef] [PubMed]

28. Chen, Z.; Zhang, L.; Sun, Y.; Hu, J.; Wang, D. 980-nm Laser-Driven Photovoltaic Cells Based on Rare-Earth Up-Converting Phosphors for Biomedical Applications. Adv. Funct. Mater. 2010, 19, 3815–3820. [CrossRef]

29. Dariva, C.G.; Coelho, J.F.J.; Serra, A.C. Near infrared light-triggered nanoparticles using singlet oxygen photocleavage for drug delivery systems. J. Control. Release 2019, 294, 337–354. [CrossRef]

30. Vankayala, R.; Hwang, K.C. Near-Infrared-Light-Activatable Nanomaterial-Mediated Phototheranostic Nanomedicines: An Emerging Paradigm for Cancer Treatment. Adv. Mater. 2018, 30, 1706320. [CrossRef]

31. Ayala-Orozco, C.; Urban, C.; Knight, M.W.; Urban, A.S.; Neumann, O.; Bishnoi, S.W.; Mukherjee, S.; Goodman, A.M.; Charron, H.; Mitchell, T.; et al. Au nanomatrystoshkas as efficient near-infrared photothermal transducers for cancer treatment: Benchmarking against nanoshells. ACS Nano 2014, 8, 6372–6381. [CrossRef] [PubMed]

32. Xu, P.; Liang, F. Nanomaterial-Based Tumor Photothermal Immunotherapy. Int. J. Nanomed. 2020, 15, 9159–9180. [CrossRef] [PubMed]

33. Zhang, W.; Ding, X.; Cheng, H.; Yin, C.; Yan, J.; Mou, Z.; Wang, W.; Cui, D.; Fan, C.; Sun, D. Dual-Targeted Gold Nanoprim for Recognition of Early Apoptosis, Dual-Model Imaging and Precise Cancer Photothermal Therapy. Theranostics 2019, 9, 5610–5625. [CrossRef]

34. Pan, L.; Liu, J.; Shi, J. Intracellular Photosensitizer Delivery and Photosensitization for Enhanced Photodynamic Therapy with Ultralow Irradiance. Adv. Funct. Mater. 2015, 24, 7318–7327. [CrossRef]

35. Prasad, R.; Chauhan, D.S.; Yadav, A.S.; Devrukhkar, J.; Singh, B.; Gorain, M.; Temigere, M.; Bellare, J.; Kundu, G.C.; Srivastava, R. A biodegradable fluorescent nanohybrid for photo-driven tumor diagnosis and tumor growth inhibition. Nanoscale 2018, 10, 19082–19091. [CrossRef] [PubMed]

36. Liu, B.J.; Lin, K.Q.; Hu, S.; Wang, X.; Lei, Z.C.; Lin, H.X.; Ren, B. Extraction of absorption and scattering contribution of metallic nanoparticles toward rational synthesis and application. Anal. Chem. 2015, 87, 1058–1065. [CrossRef]

37. Jung, H.S.; Verwilgh, P.; Sharma, A.; Shin, J.; Sessler, J.L.; Kim, J.S. Organic molecule-based photothermal agents: An expanding photothermal therapy universe. Chem. Soc. Rev. 2018, 47, 2280–2297. [CrossRef]

38. Li, J.; Rao, J.; Pu, K. Recent progress on semiconducting polymer nanoparticles for molecular imaging and cancer phototherapy. Biomaterials 2018, 155, 217–235. [CrossRef]

39. Xie, H.; Li, Z.; Sun, Z.; Shao, J.; Yu, X.P.; Guo, Z.; Wang, J.; Xiao, Q.; Wang, H.; Wang, Q.Q.; et al. Metabolizable Ultrathin Bi2Se3 Nanosheets in Imaging-Guided Photothermal Therapy. Small 2016, 12, 4136–4145. [CrossRef]

40. Chen, Y.W.; Su, Y.L.; Hu, S.H.; Chen, S.Y. Functionalized graphene nanocomposites for enhancing photothermal therapy in tumor treatment. Adv. Drug Deliv. Rev. 2016, 105, 190–204. [CrossRef]

41. Zhang, P.; Hu, C.; Ran, W.; Meng, J.; Yin, Q.; Li, Y. Recent Progress in Light-Triggered Nanotheranostics for Cancer Treatment. Theranostics 2016, 6, 948–968. [CrossRef] [PubMed]

42. Liang, P.; Mao, L.; Dong, Y.; Zhao, Z.; Sun, Q.; Mazhar, M.; Ma, Y.; Yang, S.; Ren, W. Design and Application of Near-Infrared Nanomaterial-Liposome Hybrid Nanocarriers for Cancer Photothermal Therapy. Pharmaceutics 2021, 13, 2070. [CrossRef] [PubMed]
43. Wang, X.; Zhang, J.; Li, J.; Chen, Y.; Chen, Y.; Kawazoe, N.; Chen, G. Bifunctional scaffolds for the photothermal therapy of breast tumor cells and adipose tissue regeneration. *J. Mater. Chem. B* 2018, 6, 7728–7736. [CrossRef] [PubMed]

44. Tang, Y.; Yang, T.; Wang, Q.; Lv, X.; Song, X.; Ke, H.; Guo, Z.; Huang, X.; Hu, J.; Li, Z.; et al. Albumin-coordinated assembly of clearable platinum nanodots for photo-induced cancer theranostics. *Biomaterials* 2018, 154, 248–260. [CrossRef]

45. Wang, Y.; Li; J.; Li, X.; Shi, J.; Jiang, Z.; Zhang, C.Y. Graphene-based nanomaterials for cancer therapy and anti-infections. *Bioact. Mater.* 2022, 14, 335–349. [CrossRef]

46. Lagos, K.J.; Buzzá, H.H.; Bagnato, V.S.; Romero, M.P. Carbon-Based Materials in Photodynamic and Photothermal Therapies Applied to Tumor Destruction. *Int. J. Mol. Sci.* 2021, 23, 22. [CrossRef]

47. Sun, S.; Chen, J.; Jiang, K.; Tang, Z.; Wang, Y.; Li, Z.; Liu, C.; Wu, A.; Lin, H. Ce6-Modified Carbon Dots for Multimodal-Imaging-Guided and Single-NIR-Laser-Triggered Photothermal/Photodynamic Synergistic Cancer Therapy by Reduced Irradiation Power. *ACS Appl. Mater. Interfaces* 2019, 11, 5791–5803. [CrossRef]

48. Wei, W.; Zhang, X.; Zhang, S.; Wei, G.; Su, Z. Biomedical and bioactive engineered nanomaterials for targeted tumor photothermal therapy: A review. *Mater. Sci. Eng. C Mater. Biol. Appl.* 2019, 104, 109891. [CrossRef]

49. Liang, S.; Deng, X.; Chang, Y.; Sun, C.; Shao, S.; Xie, Z.; Xiao, X.; Ma, P.; Zhang, H.; Cheng, Z.; et al. Intelligent Hollow Pt-CuS Janus Architecture for Synergistic Catalysis-Enhanced Sonodynamic and Photothermal Cancer Therapy. *Nano Lett.* 2019, 19, 4134–4145. [CrossRef]

50. Curcio, A.; Silva, A.K.A.; Cabana, S.; Espinosa, A.; Baptiste, B.; Menguy, N.; Wilhelm, C.; Abou-Hassan, A. Iron Oxide Nanoflowers with excellent photothermal properties under 808 nm excitation. *Acta Chim. Sin. Chin. Ed.* 2021, 77, 1230–1238. [CrossRef]

51. Ling, C.; Wang, X.; Shen, Y. Advances in Hollow Inorganic Nanomedicines for Photothermal-Based Therapies. *Int. J. Nanomed.* 2021, 16, 493–513. [CrossRef]

52. Zhou, J.; Chen, J.; Ge, Y.; Shao, Y. Two-dimensional nanomaterials for Förster resonance energy transfer–based sensing applications. *Nanophotonics* 2020, 9, 1855–1875. [CrossRef]

53. Liu, J.; Hao, R.; Jia, B.; Zhao, H.; Guo, L. Manipulation on Two-Dimensional Amorphous Nanomaterials for Enhanced Electrochemical Energy Storage and Conversion. *Nanomaterials* 2021, 11, 3246. [CrossRef] [PubMed]

54. Cheng, J.; Gao, L.; Li, T.; Mei, S.; Wang, C.; Wei, B.; Huang, W.; Li, C.; Zheng, G.; Wang, H.; et al. Two-Dimensional Black Phosphorus Nanomaterials: Emerging Advances in Electrochemical Energy Storage Science. *Nanomicro lett.* 2020, 12, 179. [CrossRef]

55. Chen, Y.; Fan, Z.; Zhang, Z.; Niu, W.; Li, C.; Yang, N.; Chen, B.; Zhang, H. Two-Dimensional Metal Nanomaterials: Synthesis, Properties, and Applications. *Chem. Rev.* 2018, 118, 6409–6455. [CrossRef]

56. Huang, K.; Li, Z.; Lin, J.; Han, G.; Huang, P. Correction: Two-dimensional transition metal carbides and nitrides (MXenes) for biomedical applications. *Chem. Rev.* 2018, 117, 5109–5124. [CrossRef]

57. Zhang, Y.; Lv, F.; Cheng, Y.; Yuan, Z.; Yang, F.; Liu, C.; Cao, Y.; Zheng, K.; Lu, H.; Zada, S.; et al. Pd@Au Bimetallic Nanoplates Decorated Mesoporous MnO2 for Synergistic Nucleus-Targeted NIR-II Photothermal and Hypoxia-Relieved Photodynamic Therapy. *Adv. Healthc. Mater.* 2020, 9, 1901528. [CrossRef]

58. Wang, J.; Duan, Q.; Yang, M.; Zhang, B.; Guo, L.; Li, P.; Zhang, W.; Sang, S. Rapid controlled synthesis of gold-platinum nanorods with excellent photothermal properties under 808 nm excitation. *Beilstein J. Nanotechnol.* 2021, 12, 462–472. [CrossRef] [PubMed]

59. Mahari, S.; Roberts, A.; Gandhi, S. Probe-free nanosensor for the detection of Salmonella using gold nanorods as an electroactive modulator. *Food Chem.* 2022, 390, 133219. [CrossRef]

60. Bui, D.T.; Havelek, R.; Královek, V.; Kubičková, L.; Kubičková, J.; Matouš, P.; Herynek, V.; Muthná, D.; Řezanka, P.; et al. Multimodal Contrast Agent Enabling pH Sensing Based on Organically Functionalized Gold Nanoshells with Mn-Zn Ferrite Cores. *Nanomaterials* 2022, 12, 428. [CrossRef] [PubMed]

61. Chow, T.H.; Lai, Y.; Cui, X.; Lu, W.; Zhuo, X.; Wang, J. Colloidal Gold Nanorings and Their Plasma Coupling with Gold Nanospheres. *Small* 2019, 15, 1902608. [CrossRef] [PubMed]

62. Lee, H.E.; Ahn, H.Y.; Mun, J.; Lee, Y.Y.; Kim, M.; Cho, N.H.; Chang, K.; Kim, W.S.; Rho, J.; Nam, K.T. Amino-acid- and peptide-directed synthesis of chiral plasmic gold nanoparticles. *Nature* 2018, 556, 360–365. [CrossRef] [PubMed]

63. Wang, H.; Liu, Y.; Yu, J.; Luo, Y.; Wang, L.; Yang, T.; Raktani, B.; Lee, H. Selectively Regulating the Chiral Morphology of Amino Acid-Assisted Chiral Gold Nanoparticles with Circularly Polarized Light. *ACS Appl. Mater. Interfaces* 2022, 14, 3559–3567. [CrossRef]

64. Du, B.; Ma, C.; Ding, G.; Han, X.; Li, D.; Wang, E.; Wang, J. Cooperative Strategies for Enhancing Performance of Photothermal Therapy (PTT) Agent: Optimizing Its Photothermal Conversion and Cell Internalization Ability. *Small* 2017, 13, 1603275. [CrossRef]
68. Yata, T.; Takahashi, Y.; Tan, M.; Nakatsuji, H.; Ohtsuki, S.; Murakami, T.; Imahori, H.; Umeki, Y.; Shiomi, T.; Takakura, Y.; et al. DNA nanotechnology-based composite-type gold nanoparticle-immunostimulatory DNA hydrogel for tumor photothermal immunotherapy. *Biomaterials* **2017**, *146*, 136–145. [CrossRef]

69. Liu, H.; Chen, D.; Li, L.; Liu, T.; Tan, L.; Wu, X.; Tang, F. Multifunctional gold nanoshells on silica nanorattles: A platform for the combination of photothermal therapy and chemotherapy with low systemic toxicity. *Angew. Chem. Int. Ed. Engl.* **2011**, *50*, 891–895. [CrossRef]

70. Mohammad, F.; Balají, G.; Weber, A.; Uppu, R.M.; Kumar, C.S. Influence of Gold Nanoshell on Hyperthermia of Super Paramagnetic Iron Oxide Nanoparticles (SPIONs). *J. Phys. Chem. Nanomater. Interfaces* **2010**, *114*, 19194–19201. [CrossRef]

71. Vankayala, R.; Lin, C.C.; Kalluru, P.; Chiang, C.S.; Hwang, K.C. Gold nanoshells-mediated bimodal photodynamic and photothermal cancer treatment using ultra-low doses of near infra-red light. *Biomaterials* **2014**, *35*, 5527–5538. [CrossRef] [PubMed]

72. Gazzi, A.; Fusco, L.; Khan, A.; Bedognetti, D.; Zavan, B.; Vitale, F.; Yilmazer, A.; Delongu, L.G. Photodynamic Therapy Based on Graphene and MXene in Cancer Theranostics. *Front. Bioeng. Biotech.* **2019**, *7*, 295. [CrossRef] [PubMed]

73. Gao, F.; Sun, Z.; Zhao, L.; Chen, F.; Stenzel, M.; Wang, F.; Li, H.; Zhang, L.; Jiang, Y. Bioactive engineered photothermal nanomaterials: From theoretical understanding to cutting-edge application strategies in anti-cancer therapy. *Mater. Chem. Front.* **2021**, *5*, 5257–5297. [CrossRef]

74. Popov, V.N. Carbon Nanotubes: Properties and Application. *Mater. Sci. Eng. R Rep.* **2004**, *33*, 61–102. [CrossRef]

75. Wang, X.; Li, B.; Jing, H.; Dong, X.; Leng, X. MWCNT-mediated combinatorial photothermal ablation and chemo-immunotherapy strategy for the treatment of melanoma. *J. Mater. Chem. B* **2020**, *8*, 4245–4258. [CrossRef]

76. Dong, X.; Sun, Z.; Wang, X.; Zhu, D.; Liu, L.; Leng, X. Simultaneous monitoring of the drug release and antitumor effect of a novel drug delivery system-MWCNTs/DOX/TC. *Drug Deliv.* **2017**, *24*, 143–151. [CrossRef]

77. Dong, X.; Sun, Z.; Wang, X.; Leng, X. An innovative MWCNTs/DOX/TMC nanosystem for chemo-photothermal combination therapy of cancer. *Nanomedicine* **2017**, *13*, 2271–2280. [CrossRef]

78. Zhou, M.; Liu, S.; Jiang, Y.; Ma, H.; Min, S.; Wang, Q.; Wen, Z.; Liao, W.; Xing, M. Doxorubicin-Loaded Single Wall Nanotube Thermosensitive Hydrogel for Gastric Cancer Chemo-Photothermal Therapy. *Theranostics* (2018), 337. [CrossRef] [PubMed]

79. Garcia-Valdivia, A.A.; Jannus, F.; García-García, A.; Choquesillo-Lazarte, D.; Fernández, B.; Medina-O’donnell, M.; Lupíañez, J.A.; Cepeda, J.; Reyes-Zurita, F.J.; Rodríguez-Díegez, A. Anti-cancer and anti-inflammatory activities of a new family of coordination compounds based on divalent transition metal ions and indazole-3-carboxylic acid. *J. Inorg. Biochem.* **2021**, *215*, 111308. [CrossRef]

80. Gill, M.R.; Vallis, K.A. Transition metal compounds as cancer radiosensitizers. *Chem. Soc. Rev.* **2019**, *48*, 540–557. [CrossRef]

81. Presutti, D.; Agarwal, T.; Zarepour, A.; Celikkin, N.; Hooshmand, S.; Nayak, C.; Ghomi, M.; Zarrabi, A.; Costantini, M.; Behera, B.; et al. Transition Metal Dichalcogenides (TMDC)-Based Nanozymes for Biosensing and Therapeutic Applications. *Materials* **2022**, *15*, 337. [CrossRef] [PubMed]

82. Li, Z.; Yu, Y.; Zeng, W.; Ding, F.; Zhang, D.; Cheng, W.; Wang, M.; Chen, H.; Pan, G.; Mei, L.; et al. Mussel-Inspired Ligand Clicking and Ion Coordination on 2D Black Phosphorus for Cancer Multimodal Imaging and Therapy. *Small* **2022**, *18*, 2201803. [CrossRef] [PubMed]

83. Fang, Y.; Zhang, Z.; Liu, Y.; Gao, T.; Liang, S.; Chu, Q.; Guan, L.; Mu, W.; Fu, S.; Yang, H.; et al. Artificial Assembled Macrophage Co-Deliver Black Phosphorus Quantum Dot and CDK4/6 Inhibitor for Colorectal Cancer Triple-Therapy. *ACS Appl. Mater. Interfaces* **2022**, *14*, 20628–20640. [CrossRef]

84. Lu, B.; Hu, S.; Wu, D.; Wu, C.; Zhu, Z.; Hu, L.; Zhang, J. Ionic liquid exfoliated Ti3C2Tx MXene nanosheets for photoacoustic imaging and synergistic photothermal therapy of cancer. *J. Mater. Chem. B* **2022**, *10*, 1226–1235. [CrossRef]

85. Sadiq, M.; Pang, L.; Johnson, M.; Sathish, V.; Zhang, Q.; Wang, D. 2D Nanomaterial, Ti3C2Tx MXene-Based Sensor to Guide Lung Cancer Therapy and Management. *Biosensors* **2021**, *11*, 40. [CrossRef]

86. Liu, Z.; Zhao, M.; Lin, H.; Dai, C.; Ren, C.; Zhang, S.; Peng, W.; Chen, Y. 2D magnetic titanium carbide MXene for cancer theranostics. *J. Mater. Chem. B* **2018**, *6*, 3541–3548. [CrossRef]

87. Zhang, A.; Li, A.; Zhao, W.; Liu, J. Recent Advances in Functional Polymer Decorated Two-Dimensional Transition-Metal Dichalcogenides Nanomaterials for Chemo-Photothermal Therapy. *Chemistry* **2018**, *24*, 4215–4227. [CrossRef] [PubMed]

88. Wu, J.; Bremner, D.H.; Niu, S.; Wu, H.; Wu, J.; Wang, H.; Li, H.; Zhu, L.-M. Functionalized MoS2 nanosheet-capped periodic mesoporous organosilicas as a multifunctional platform for synergistic targeted chemo-photothermal therapy. *Chem. Eng. J.* **2018**, *342*, 90–102. [CrossRef]

89. Liu, Y.; Peng, J.; Wang, S.; Xu, M.; Gao, M.; Xia, T.; Weng, J.; Xu, A.; Liu, S. Molybdenum disulfide/graphene oxide nanocomposites show favorable lung targeting and enhanced drug loading/tumor-killing efficacy with improved biocompatibility. *NPJ Asia Mater.* **2018**, *10*, e458. [CrossRef]

90. Zhou, Z.; Song, Q.; Huang, B.; Peng, S.; Lu, C. Facile Fabrication of Densely Packed Ti3C2Tx MXene/Nanocellulose Composite Films for Enhancing Electromagnetic Interference Shielding and Electro-/Photothermal Performance. *ACS Nano* **2021**, *15*, 12405–12417. [CrossRef]

91. Xu, D.; Li, Z.; Li, L.; Wang, J. Insights into the Photothermal Conversion of 2D MXene Nanomaterials: Synthesis, Mechanism, and Applications. *Adv. Funct. Mater.* **2020**, *30*, 2000712. [CrossRef]

92. Liu, Z.; Lin, H.; Zhao, M.; Dai, C.; Zhang, S.; Peng, W.; Chen, Y. 2D Superparamagnetic Tantalum Carbide Composite MXenes for Efficient Breast-Cancer Theranostics. *Theranostics* **2018**, *8*, 1648–1664. [CrossRef] [PubMed]
93. Lin, H.; Gao, S.; Dai, C.; Chen, Y.; Shi, J. A Two-Dimensional Biodegradable Niobium Carbide (MXene) for Photothermal Tumor Eradication in NIR-I and NIR-II Biowindows. *J. Am. Chem. Soc.* 2017, 139, 16235–16247. [CrossRef] [PubMed]

94. Li, R.; Zhang, L.; Shi, L.; Wang, P. MXene Ti$_3$C$_2$: An Effective 2D Light-to-Heat Conversion Material. *ACS Nano* 2017, 11, 3752–3759. [CrossRef] [PubMed]

95. Chen, W.; Ouyang, J.; Liu, H.; Chen, M.; Zeng, K.; Sheng, J.; Liu, Z.; Han, Y.; Wang, L.; Li, J.; et al. Black Phosphorus Nanosheet-Based Drug Delivery System for Synergistic Photodynamic/Photothermal/Chemotherapy of Cancer. *Adv. Mater.* 2017, 29, 1603864. [CrossRef]

96. Xing, C.; Chen, S.; Li, H.; Gao, S.; Dai, C.; Chen, Y.; Shi, J. A Two-Dimensional Biodegradable Niobium Carbide (MXene) for Photothermal Tumor Therapy. *J. Mater. Chem. B* 2021, 9, 7909–7926. [CrossRef]

97. Cadonà, E.C.; Dantas, R.F.; de Mello, G.H.; Silva-Jr, F.P. Natural products targeting into cancer hallmarks: An update on caffeine, theobromine, and (+)-catechin. *Crit. Rev. Food Sci. Nutr.* 2021. [CrossRef] [PubMed]

98. Yz, A.; Fang, F.B.; Yc, C.; Min, L.B.; Li, L.A.; Wl, D.; Jz, B. Hollow Mesoporous Polyaniline Nanoparticles with High Drug Payload and Robust Photothermal Capability for Cancer Combination Therapy. *Front. Pharmacol.* 2021, 12, 212–228. [CrossRef]

99. Wang, S.; Ma, Z.; Shi, Z.; Huang, Y.; Chen, T.; Hou, L.; Jiang, T.; Yang, F. Chidamide stacked in magnetic polypropylene nanocomposites counter thermotolerance and metastasis for visualized cancer photothermal therapy. *Drug Deliv.* 2022, 29, 1312–1325. [CrossRef]

100. Li, M.; Teh, C.; Ang, C.Y.; Tan, S.Y.; Luo, Z.; Qu, Q.; Zhang, V.; Korzh, V.; Zhao, Y. Near-Infrared Light-Absorptive Stealth Liposomes for Localized Photothermal Ablation of Tumors Combined with Chemotherapy. *Adv. Funct. Mater.* 2021, 31, 2004788. [CrossRef] [PubMed]

101. Kim, N.Y.; Blake, S.; De, D.; Ouyang, J.; Shi, J.; Kong, N. Two-Dimensional Nanosheet-Based Photonic Nanomedicine for Combined Gene and Photothermal Therapy. *Chem. Eng. Mater.* 2019, 38, 212–228. [CrossRef]

102. Lu, J.; Cai, L.; Dai, Y.; Liu, Y.; Zuo, F.; Ni, C.; Shi, M.; Li, J. Polypyrrole-Based Nanomaterials for Photothermal Therapy/Chemotherapy and their Synergistic Therapy with Autophagy Inhibitor to Promote Antitumor Treatment. *Chem. Rec.* 2021, 21, 781–796. [CrossRef]

103. Sun, H.; Zhang, Q.; Li, J.; Peng, S.; Cai, R. Near-infrared photoactivated nanomedicines for photothermal synergistic cancer therapy. *Nano Today* 2021, 37, 101073. [CrossRef]

104. Peng, T.; Xu, T.; Liu, X. Research progress of the engagement of inorganic nanomaterials in cancer immunotherapy. *Drug Deliv.* 2022, 29, 1914–1932. [CrossRef] [PubMed]

105. Chang, M.; Hou, Z.; Wang, M.; Li, C.; Lin, J. Recent Advances in Hyperthermia Therapy-Based Synergistic Immunotherapy. *Adv. Mater.* 2021, 33, 2004788. [CrossRef] [PubMed]

106. Jianhua, Z.; Ling, L.; Zhen, Y.; Xiaoyuan, C. Phototherapy meets immunotherapy: A win–win strategy to fight against cancer. *Nanophotonics* 2021, 10, 3229–3245. [CrossRef]

107. Wang, C.; Xu, L.; Liang, C.; Xiang, J.; Peng, R.; Liu, Z. Immunological responses triggered by photothermal therapy with carbon nanotubes in combination with anti-CTLA-4 therapy to inhibit cancer metastasis. *Adv. Mater.* 2014, 26, 8154–8162. [CrossRef]

108. Zhou, F.; Li, X.; Naylor, M.F.; Hode, T.; Nordquist, R.E.; Alleruzzo, L.; Raker, J.; Lam, S.S.; Du, N.; Shi, L.; et al. InCVAX—A novel strategy for treatment of late-stage, metastatic cancers through photoinmunotherapy induced tumor-specific immunity. *Cancer Lett.* 2015, 359, 169–177. [CrossRef]

109. Chen, J.; Ning, C.; Zhou, Z.; Yu, P.; Zhu, Y.; Tan, G.; Mao, C. Nanomaterials as photothermal therapeutic agents. *Prog. Mater. Sci.* 2019, 99, 1–26. [CrossRef]
117. Li, Z.; Chen, Y.; Yang, Y.; Yu, Y.; Zhang, Y.; Zhu, D.; Yu, X.; Ouyang, X.; Xie, Z.; Zhao, Y.; et al. Recent Advances in Nanomaterials-Based Chemo-Photothermal Combination Therapy for Improving Cancer Treatment. *Front. Bioeng. Biotech.* 2019, 7, 293. [CrossRef]

118. Chen, Y.-W.; Chen, P.-J.; Hu, S.-H.; Chen, I.-W.; Chen, S.-Y. NIR-Triggered Synergic Photo-chemothermal Therapy Delivered by Reduced Graphene Oxide/Carbon/Mesoporous Silica Nanocookies. *Adv. Funct. Mater.* 2014, 24, 451–459. [CrossRef]

119. Wang, L.; Shi, J.; Jia, X.; Liu, R.; Wang, H.; Wang, Z.; Li, L.; Zhang, J.; Zhang, C.; Zhang, Z. NIR-/pH-Responsive drug delivery of functionalized single-walled carbon nanotubes for potential application in cancer chemo-photothermal therapy. *Pharm. Res.* 2013, 30, 2757–2771. [CrossRef]

120. Hou, W.; Liu, Y.; Jiang, Y.; Wu, Y.; Cui, C.; Wang, Y.; Zhang, L.; Teng, I.T.; Tan, W. Aptamer-based multifunctional ligand-modified UCNPs for targeted PDT and bioimaging. *Nanoscale* 2018, 10, 10986–10990. [CrossRef]

121. Celli, J.P.; Spring, B.Q.; Rizvi, I.; Evans, C.L.; Samkoe, K.S.; Verma, S.; Pogue, B.W.; Hasan, T. Imaging and photodynamic therapy: Mechanisms, monitoring, and optimization. *Chem. Rev.* 2010, 110, 2795–2838. [CrossRef] [PubMed]

122. Kim, J.; Cho, H.R.; Jeon, H.; Kim, D.; Song, C.; Lee, N.; Choi, S.H.; Hyeon, T. Continuous O₂-Evolving MnFe₂O₄ Nanoparticle-Anchored Mesoporous Silica Nanoparticles for Efficient Photodynamic Therapy in Hypoxic Cancer. *J. Am. Chem. Soc.* 2017, 139, 10992–10995. [CrossRef] [PubMed]

123. Chu, C.; Lin, H.; Liu, H.; Wang, X.; Wang, J.; Zhang, P.; Gao, H.; Huang, C.; Zeng, Y.; Tan, Y.; et al. Tumor Microenvironment-Triggered Supramolecular System as an In Situ Nanotheranostic Generator for Cancer Phototherapy. *Adv. Mater.* 2017, 29, 1605928. [CrossRef] [PubMed]

124. Zheng, N.; Chen, Y.; Jiang, L.; Ma, H. Fabrication of denatured BSA-hemin-IR780 (dBHI) nanoplatform for synergistic combination of phototherapy and chemodynamic therapy. *Colloids Surf.* 2021, 634, 127957. [CrossRef]

125. Taratula, O.; Schumann, C.; Duong, T.; Taylor, K.L.; Taratula, O. Dendrimer-encapsulated naphthalocyanine as a single agent-based theranostic nanoplatform for near-infrared fluorescence imaging and combinatorial anticancer phototherapy. *Nanoscale* 2015, 7, 3888–3902. [CrossRef]