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REVIEW ARTICLE

Nanotechnology Potent Photothermal and Photodynamic Immunotherapies of Cancer

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Abstract

Purpose Nano-photosensitizer-based light-activated treatments are safe for numerous cancer indications. Photodynamic therapy (PDT) induces chemical damage to targeted lesions, and photothermal therapy (PTT) causes thermal damage. PTT contrast agents are not required for PDT, but they can boost their effectiveness. PDT uses photosensitizers. Phototherapies based on nanoparticles exhibit high efficacy, limited invasion, and few harmful effects when used to treat cancers. This review discusses phototherapies for cancer therapy and developing preclinical methodologies that may improve their effectiveness and utility.

Methods All the reported works were retrieved from two databases (i.e., PubMed and Google Scholar) using the keywords "Photothermal therapy" "immunotherapy", "cancer", "nanoparticles", and "photodynamic therapy". This paper surveyed studies on nanoparticle-based photo/immunotherapies and examined recent nanoparticle-based PTT and PDT developments. We also will be discussed difficulties and potential future research areas.

Results Recent research has focused on these phototherapies. Phototherapeutic devices and drugs have been evolved recently for cancer treatments, however, considerable difficulties have limited their clinical use to a few dermatological disorders. Combining nano-based photosensitizers with chemotherapies or immunotherapies for targeting or localizing activation could improve outcomes and reduce adverse effects.

Conclusion These innovative approaches are anticipated to play a significant role in advancing conventional tumor therapy approaches.

Keywords Photothermal Therapy · Photodynamic Therapy · Nanoparticles · Immunotherapy · cancer

1 Introduction

Radiation therapy, chemotherapy, molecular targeted therapy, and immunotherapy are a few of the several anticancer treatment modalities that have seen significant growth in recent years. But each year has seen a steady rise in the incidence and death of malignancies, and rising trend in the number of young cancer patients [1]. The absence of unpleasant and efficient therapeutic options is critical in this

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phenomenon. Therefore, it is imperative to create new, effective anticancer therapies.

In the last ten years, cancer immunotherapy has made enormous strides [2, 3]. For instance, the development of oncology therapies has been greatly aided by the effectiveness of immune checkpoint inhibitors (e.g., anti-PD-1/PD-L1 and anti-cytotoxic T lymphocyte-associated antigen-4) antibodies [4–6]. These advancements have produced various integrated treatment programs using multiple therapeutic modalities (i.e., chemo/immunotherapy, radio/immunotherapy, and targeted molecular/immunotherapy) [7–10]. Nevertheless, recent investigations have revealed that these "miracle medications" were useless for cancers and displayed variable therapeutic efficacy in different patients [11]. The clinical optimization of these techniques has also been challenged by adverse immunological effects, such as the impact on the inflammatory mediator's cascade, toxicity in the target organ, hematological system malfunction, and inducing drug resistance [12–15].

Consequently, one important aim is to increase the effectiveness of immunotherapeutic medications and decrease their adverse effects. Research into novel cancer therapy methods is ongoing. Malignant tumors are currently being treated in clinics using a variety of tumor ablations, including thermal, cryo, microwave, and ultrasonic ablations, distinguished by less trauma, controllability, and deaths in targeted sites [16]. The subsequent tumor cell death during tumor ablation can be the potential antigen source to stimulate the immune response for direct killing [17]. Both primary and metastatic cancers can be treated with thermal ablation by inducing an immune response.

The fundamental mechanism in pre-clinical and clinical investigations is that damaged tumorous cells release specific antigens (tumor-associated antigens) and can stimulate the systemic response [18]. In contrast to traditional anticancer techniques, nanostructures-based PTT/PDT are cutting-edge treatment alternatives for tumor erosion. The applicability of ablations is further expanded using nanoparticles, which incorporate the benefits of nanomedicine (e.g., drug-loading, targeting, versatility, and modifiability) into tumor ablation [19, 20]. Nanoparticle-based PTT and PDT immunotherapies, can generate lasting antitumor immune responses and remove tumors by ablation.

2 Pathological Mechanism Tumor Cells Death by PTT and PDT

Heat shock proteins (HSPs), particularly HSP70, are widely distributed molecular chaperones that facilitate proper protein folding and exhibit enhanced expression at elevated temperature conditions [21, 22]. Hsp70 has an antiapoptotic influence through its ability to impede the activation of caspase-3 and hinder the stress-activated kinase pathway [23]. The complex formation of anti-apoptosis-related proteins can be reduced by down-regulation of HSP70 and BAG3. Wang et al. demonstrated that CTD-TSL@GNPs, by inhibiting HSP induced by PTT and weakening the antiapoptotic signal, achieved a practical PTT effect on A431 cells. Furthermore, the irradiation power used in this study was clinically acceptable [24]. Based on prior research, it has been observed that the suppression of HSP activity can disrupt cellular homeostasis and compromise the integrity of protein interactions. Consequently, this disruption leads to a decrease in cell thermotolerance and an enhancement in the efficacy of photothermal therapy [25]. According to Moustafa R.K. Ali et al., the HSP70 level in Huh7.5 cells was around one-tenth of that observed in HSC and MCF-7 cells when considering the relative level and resulting outcomes. In contrast to the other two cell lines, the induction of programmed cell death (apoptosis) in Huh7.5 cells exhibited a notable and statistically significant increase following exposure to PPT [21]. Consequently, targeting HSP70 suppression has been acknowledged as a viable approach in cancer therapy since it can potentially render cancer cells more susceptible to PTT. Hsp72 is a prominent constituent of the molecular chaperone family as well. In contrast to the reduced expression observed in normal cells, the expression level in tumor tissues exhibited a substantial rise, presumably as a protective mechanism against apoptotic induction. Wang et al. developed a nanoscale system comprising HSP72 /hyaluronic acid and gold nanostare/siRNA. This system was effectively fabricated using the layer-by-layer technique [26]. The JAK/STAT signaling pathway, particularly the STAT3 protein, plays a significant role in the initiation and progression of carcinogenesis and development through its regulation of the TARGE gene. The cell cycle regulators, namely c-fos, meks, cMyc, and cyclinD1, and the apoptosis inhibitors, including Survivin and Bcl-xL, are rapid signal transduction pathways facilitating communication from the extracellular environment to the nuclear compartment. The oncogenic nature of STAT3 is evident, as its activation and overexpression are closely associated with the malignant conversion of cells [27]. The Bcl-2 family is categorized into two distinct subfamilies in the context of apoptosis. There exist anti-apoptotic proteins, such as START3 downstream target genes Bcl-2 and Bcl-xl, that experience conformational alterations as they transition from the cytoplasm to the organelles within the membrane structure, particularly the outer membrane of the mitochondria. These changes occur when cells are stimulated by death signals and pro-apoptotic proteins Bax and Bak, respectively, in the case of a cell in a stable condition [28]. The experimental findings demonstrated that the overexpression of STAT3 had a notable mitigating effect on the inhibitory impact of ALA-PDT [29]. The cellular uptake of the molecule STAT3 dimer,

dependent on both dose and light exposure, has emerged as a valuable indicator of the effectiveness of PDT in laboratory settings and living organisms. This compound can serve as a biomarker to assess and enhance the therapeutic characteristics of existing and potential PDT candidates in vivo. Li et al., the integration of ALA-PDT with STAT3 siRNA demonstrates favorable tumor tissue selectivity, absence of discomfort, and absence of scar formation in the treatment of squamous cell carcinoma [30]. The EGFR receptor tyrosine kinase plays a crucial role in safeguarding against apoptosis by regulating essential cellular processes like phosphatidylinositol 3'kinase (PI3K)/AKT signaling, cell cycle progression and survival through proliferation, as well as MAPK and STAT3 pathways [28]. In addition to her findings, Christine edmonds observed that PDT induces the activation of tyrosine phosphorylation and subsequent nuclear translocation of the EGFR. Hence, the concurrent administration of erlotinib, an inhibitor of the EGFR signal, with PDT can potentially enhance the cytotoxic effects of PDT through the up-regulation of the apoptotic cell death pathway [31]. To effectively engage the body's immune system and address residual tumor cells and metastatic cancer, combining PTT with supplementary immune interventions is necessary. This approach facilitates activating and coordinating the body's comprehensive immune response. Zhou et al. have also devised an interventional photothermal therapy method incorporating immune adjuvants. According to reports, chitosan is identified as the precursor of GC. Its effects include the promotion of DC maturation through the induction of a type I interferon-induced antigen-specific Th1 response. Additionally, chitosan can increase the release of interferon-γ and tumor necrosis factor-α. However, further investigation is required to evaluate the immunomodulatory activity of GC in other studies [32]. The enhanced maturation of dendritic cells induced by the AlBSA-Ce6NPs created by Yining Zhu results in increased infiltration of tumors and lymph nodes by $CD8^+$ and $CD4^+$ T cells. This approach seeks to combat melanoma by utilizing albumin-biomineralized nanoparticles to synergize PTT with immunotherapy [33].

3 Nanomaterial-Based Photothermal Therapy

A breakthrough approach called photothermal therapy (PTT) based on nanoparticles uses the conversion of light energy to heat-induced cancer cells killing. The following distinctive characteristics of PTT stand out compared to current standard therapies. Using a local fixed-point near-infrared (NIR) laser that can penetrate muscle tissue is ideal for treating solid tumors, especially superficial tumors, without suffering from severe side effects [34, 35]. (ii) Nanoparticles with targetability can deliver therapeutic precisely eradicate malignancies after intravenous injection [36, 37]. (iii) Fluorescence, magnetic resonance, CT, and photoacoustic imaging with theranostic nanostructures all permit imaging-guided PTT [38, 39]. (iv) The use of PTT in conjunction with interventional technologies has been effectively extended to deep tumors in addition to surface cancers (such as pancreatic cancer) [40].

The development from organic to inorganic photothermal nanomaterials, from a PTT to multifunctional nanotheranostics, and from single heat production to dual efficacy and biosafety nanotechnology are examples advancements that have undergone ongoing in nanoparticle applications. To our knowledge, PTT's anticancer effects in tumor therapy primarily come from direct thermal ablation (over 42 C). Heat can physically harm the tumorous cells by rupturing the cell membrane, preventing DNA synthesis, and disrupting the cytoskeleton [41, 42]. To increase the hyperthermia temperature, researchers frequently increase the irradiation light's intensity or the number of photothermal agents used, improving tumor ablation. However, non-neoplastic tissues risk injury from agent dose or excessive laser power. Low-power radiation treatment combined with the exact targeting of subcellular components may effectively cure this issue. For instance, mitochondria-targeting nanoparticles can significantly lower the NIR power density after PTT while increasing intracellular reactive oxygen species (ROS) amounts, leading to mitochondrial dysfunction and inducing apoptosis [43, 44]. Pan et al. designed nuclear-targeting nanoparticles that may cause tumor cells to undergo apoptosis by damaging nuclear DNA and preventing DNA repair when exposed to a weak NIR laser of 0.2 W/cm^2 [45].

In response to the stress stimuli (e.g., heat, ischemia, heavy metals, and toxins), to repairing the damaged protein and prevent cell death protein shock proteins (HSPs) are overexpressed [46, 47]. Tumor cells have a high heat tolerance, this action may ultimately cause PTT to be delayed or perhaps fail. As a result, inhibiting HSPs, which are closely related to heat resistance can increase PTT's effectiveness. In general, HSP inhibitors or RNA interference agents are picked [48]. Yang and colleagues designed a PEG-modified nanofibers loaded with a HSP inhibitor to downregulate HSP90 and go around the tumor cells' heat resistance in PTT [49]. Wang et al. gold nanoshells were used to deliver HSP70 siRNA in vitro and in vivo, inhibiting HSP70 expression and specifically sensitizing PTT efficacy on tumors with few side effects [50]. Quercetin, an HSP70 siRNA and HSP70 inhibitor, was employed by Ali et al. to improve gold nanorod-based PTT. They were pleased with the findings, which included a strong cytotoxic effect on various tumor tissues at low laser intensity [21]. HSP70 is amplified due to the inhibition of HSP90 expression, which is terrible for PTT improvement. On the other hand, HSP90 expression

decreases and does not increase when HSP70 is inhibited [51, 52]. As a result, the efficiency of HSP70 inhibitors in tumor PTT may be excellent.

Addressing the limitation of siRNA and HSP inhibitors, HSP synthesis at its source should be suppressed (Such as the poor targeting, excellent stability, and good safety of siRNA, as well as the HSP inhibitors' lonesome nature and hysteresis effect). Chen and colleagues used photo-convertible nanocarriers to loading of glucose transporter inhibitor (GTI) to target tumor tissues through the interaction of hyaluronic acid and CD44. The GTI prevents glucose transfer, which prevents glycolysis, lowers ATP generation, and ultimately lowers the level of HSP expression [48].

PTT has potential anticancer effects in addition to the cell necrosis and apoptosis brought on by hyperthermia (Fig. 1). For instance, PTT shows exceptional excellence in eliminating medication resistance. PTT monotherapy cannot improve the tumor therapy resistance that induced by drug-efflux transporters or multidrug resistance [53]. Additionally, PTT can make tumors' MDR disappear. It is generally accepted that the MDR of numerous malignancies is caused by the overexpression of multidrug resistance-associated protein 1 (MRP1) and p-glycoprotein (p-gp) [54]. Li and collagenous claim that cyanine-loaded nanostructures-based PTT can reduce MRP1 and decrease the drug resistance [55]. According to Wang et al., PTTs based on carbon and gold nanoparticles can solve the DOX resistance by encouraging the expression of the HSP factor, which prevents the synthesis of p-gp [56, 57]. Additionally, PTT can increase chemo-sensitive tumor cell by potentially damaging membrane integrity following PTT, which raises the concentration of the medication in the tumor [58].

3.1 Immune Checkpoint Inhibition in Conjunction with PTT

The biggest obstacle to treating tumors is metastasis. Chemotherapy is the most popular and last resort after substantial metastasis, despite its poor effectiveness and severe side effects [59]. Using the immune system to fight metastatic cancers is a potential alternative. Incorporating immunological adjuvants with nanoparticle-based PTT can increase immune cell infiltration at tumor areas, activate both general and specific immune responses, and trigger inflammatory factors' release. Several investigations have lately shown that the inhibitory action of PTT single is insufficient to prevent the growth of primary tumors and, even more so, to prevent the spread of distant metastatic cancers [60]. Another challenge for anticancer immunotherapy is the competing interactions of cancer cells and the immune system. Cancer cells seem to be immune-tolerant/even immune-dependent in some circumstances. For example, several antitumor immunological negative regulatory signals, including CTLA-4 on regulatory T (Treg), PD-1/PD-L1, and CD47 or signal regulatory protein (SIRP), hinder immune cells from performing their primary purpose of curing cancer [61]. This leads to

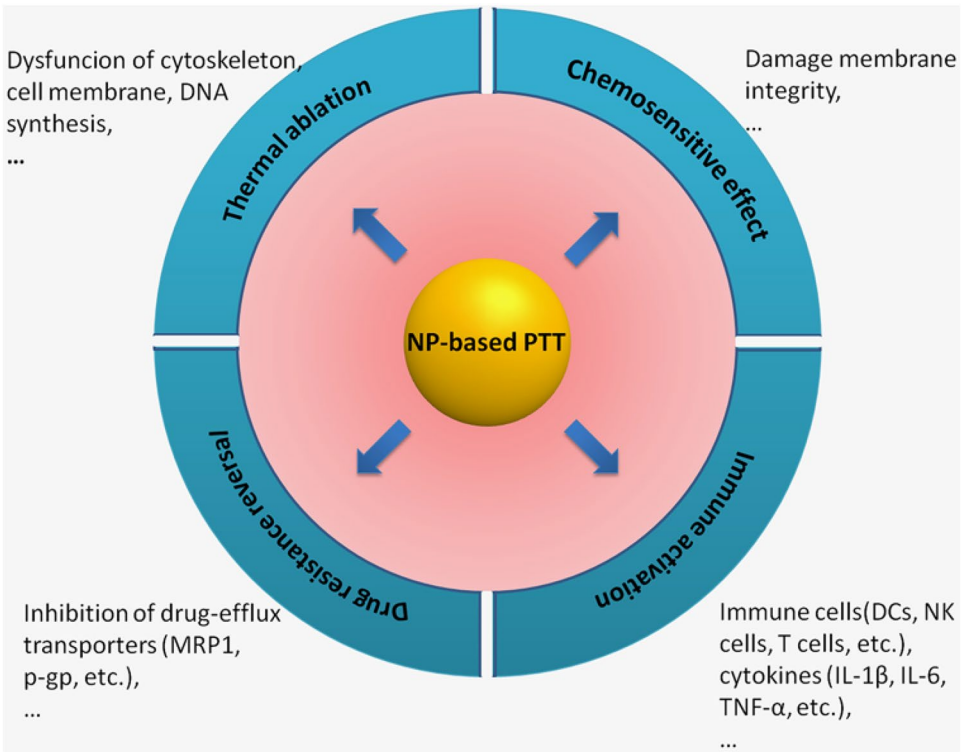

Fig. 1 Shows the antitumor effects of PTT based on nanoparticles (NP) .[https://doi.org/10.1002/ijc.31717].

Table 1 Photothermal and photodynamic therapy agents combined with immune checkpoint blockade for photo/immunotherapy

PTT/PDT	Nanoparticle	Checkpoint blockade	Effector cells	Cytokines	Tumors	Ref
PTT Agent	Prussian blue nanoparticle	Anti-CTLA-4	CD4+/CD8 + T cells		Neuroblastoma	[65]
	PEGylated carbon nanotubes	Anti-CTLA-4	DCs,$CD4^+/CD8^+$ T cells, $CD20^+$	IL-12, IL-1β, IL-6, TNF-α	Murine, breast, and melanoma	[60]
	PLGA-ICG-R837	Anti-CTLA-4	DCs,$CD4^+/CD8^+$ T cells,	IL-12, IL-1β, IL-6, TNF-α, IFN-γ	Murine, breast, and colorectal cancer	[62]
	Gold nanostar	Anti-PD-L1	$CD4^+/CD8^+$, T cells		Bladder tumor	[63]
PDT Agent	H-MnO_2-PEG/C&D	Anti-PD-L1	Macrophage, T lymphocytes	IL-12, IFN-γ, TNF-α	Murine and breast tumor	[66]
	(UCNP)-Ce6-R837	Anti-CTLA-4	DCs, $CD4^+/CD8^+$ T cells,	IL-12, IFN-γ, TNF-α	murine and colorectal cancer	[67]
	NCP@pyrolipid	Anti-PD-L1	$CD4^+/CD8^+$ T cells	IFN-γ, TNF-α	Murine and colorectal cancer	[68]
	(ZnP@pyro)	Anti-PD-L1	Macrophage, DCs	IL-6, IFN-γ, TNF-α	Murine and breast tumor	[69]
	(IDOi)@TBC-Hf	Indoleamine 2,3-dioxygenase inhibitor (IDOi)	Neutrophils, B, NK and cells, DCs,	IFN-γ	Murine and colorectal tumor	[70]

the failure of immunotherapy. These mechanisms are the main barriers to the use and advancement of photothermal immunotherapy. Therefore, reducing these unfavorable signals can enhance PTT's therapeutic effects. Photothermal therapy with SWNTs raises the proportion of $CD4^+$ immune cells, according to Wang et al. This may partially suppress antitumor immunity. Treatment with anti-CTLA-4 can lower the number of Treg and, inadvertently, boost the ability of T cells to kill local and distant tumors. Coupling anti-CTLA-4 with organic nanocomposite PTT made of PLGA-ICGR837 has a more substantial suppressive impact on distant tumors [60].

Nano-formulated drugs can accumulate in tumor sites by passive or active targeting strategies; thus, light and heat radiation can better kill tumor cells. The debris and associated antigens of tumor cells cause the innate immune system to become more active, killing any remaining or metastatic tumors (Fig. 2). Dendritic cells (DCs) the most

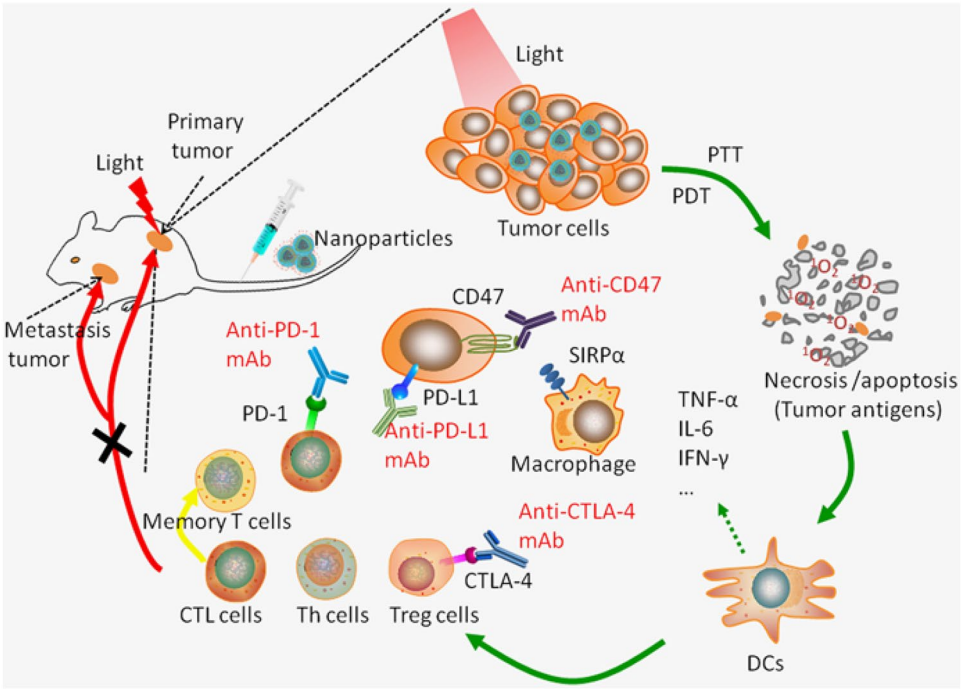

Fig. 2 Nanomaterial-based PTT and PDT-induced antitumor immune responses. Through either passive or aggressive targeting, nanoparticles reach the tumor site. PTT or PDT both kill tumor cells. Then, cell debris and tumor-associated antigens are released to activate immune effector cells, including DCs and T lymphocytes, and cause them to be redistributed. These immune effector cells also express and secrete cytokines. Checkpoint inhibitors can improve antitumor immunity when used in combinatorial forms to treat both primary and metastatic cancers [https://doi.org/10.1002/ijc.31717].

powerful and classical antigen presenting cells (APCs) that effectively phagocytose, process, and transmit tumor antigens throughout this process. Mature DCs release cytokines that further activate the T cell-mediated adaptive immune system or draw in macrophages and NK cells. Additionally, this combined therapy encourages the development of memory T cells, which prevents tumor recurrence and results in long-term tumor-free survival [62]. For the treatment of bladder cancer, gold nanostar-based PTT using anti-PD-L1 has been investigated. These findings support the notion that this combination therapy, which involves immune stimulation and the removal of the tumor's defenses before heat ablation, can effectively treat both local and distant cancers [63]. Table 1 provides more information and a list of other existing combination therapies. The expression of PD-L1 in a tumor microenvironment can be enhanced by anti-CTLA-4 monotherapy, which is anticipated to impair T cell-mediated antitumor immunity [64]. Therefore, it is advisable to employ anti-CTLA-4 and anti-PD-1 in combination.

Numerous clinical trials have shown that combining anti-CTLA-4 and anti-PD-1 can enhance therapeutic effects in small-cell sarcoma, melanoma, and lung cancer compared to anti-PD-1 or anti-CTLA-4 monotherapy [71–74]. However, concurrent administration of anti-CTLA-4 and anti-PD-1 along with PTT hastens the demise of tumor-bearing mice46, probably due to the combined therapy's propensity to result in grade 3 or 4 treatment-related side events [75]. This finding demonstrates the importance of considering immunotherapy's complexity and safety assessment.

4 Nanomaterial-Based Photodynamic Therapy

PDT is a clinical procedure with minimal harmful side effects, few invasive side effects, high selectivity, high reproducibility, and other benefits [76]. It is a potentially effective therapy for some cancers [77–80]. Photosensitizers (PSs) can keep in tumor tissues by a wavelength of stimulus light in the presence of O2 to form singlet oxygen and ROS, which cause the killing of the cancer cells and become necrotic [81]. The effectiveness of PDT is constrained by three crucial factors: PS, excitation light, and oxygen. A novel therapeutic approach called nanoparticle-based PDT uses nanomaterials as a carrier or PSs. Due to the distinctive characteristics of nanoparticles, nanostructure-based PDT has broadened the scope of classic PDT, fostering its advancement and increasing its applications (Fig. 3).

Traditional PSs are quickly impacted by the body's internal environment and substances, poorly soluble, unstable, and untargeted [82]. PSs' stability and biocompatibility are enhanced by targeted molecule-modified nanocarriers carrying PS to the targeting of cancer cells to enhance the therapeutic effect and lessen adverse effects [77, 83]. The short wavelength of the excitation light, primarily in the UV or visible area, resulting in minimal penetration depth and easy distribution by various endogenous light chromophores, including melanin, is another disadvantage of conventional PDT [84]. New PSs, like NIR fluorescent dyes, have been created to address the drawbacks of the PS that needed a small wavelength of excitation. The multipurpose PS ICG, IR820, and IR780 rely on NIR laser irradiation for

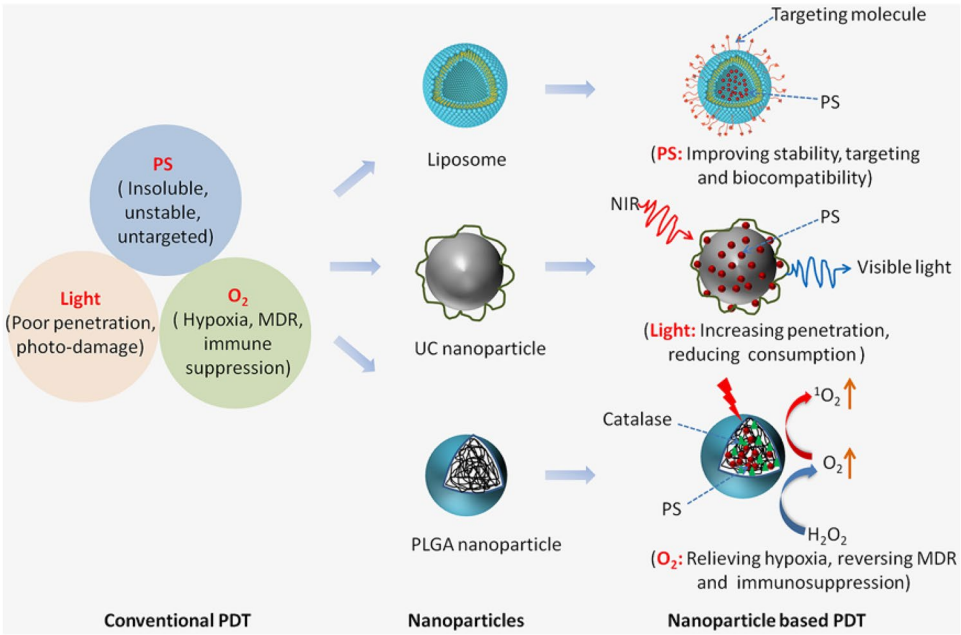

Fig. 3 PDT using nanoparticles to treat cancer more effectively [https://doi.org/10.1002/ijc.31717].

increased PDT penetration and efficacy [85–87]. Additionally, these PSs exhibit robust PTT effects and fluorescence imaging capabilities, confirming the breadth of their prospective uses in cancer therapy. Common nanomaterials like gold nanostructures, which used acclaimed for their excellent PTT impact, can help PDT. Vankayala et al. claim that gold nanorods subjected to NIR light can produce singlet oxygen and have a powerful PDT. These findings support controlled tumor therapy because they demonstrate that by adjusting the excitation light wavelength, nanorods can prevent whether PDT or PTT predominates during the treatment [88].

Another effective method is using upconversion nanomaterials to change long-wavelength light stimulation into short-wavelength. Traditional PS-dependent wavelength excitation can replace NIR light with powerful tissue penetrating characteristics when using upconversion nanoparticles [89]. Gulzar and co-workers employed graphene oxide (GO) as a carrier for chlorine-6 to use as an imaging-guided PDT agent [90]. Li and coworkers designed Nd^{3+}-lanthanide nanostructures loaded with PS to address the shortcomings of conventional Yb^{3+} ions-sensitized upconversion nanoparticles and achieve successful image-guided PDT without diminishing imaging signals [91]. Because solid tumors consume more oxygen than they produce, the hypoxic tumor microenvironment (TME) limits the effectiveness of PDT [92]. The effectiveness of PDT can be improved by increasing the oxygen amount in the tumor site. Hyaluronidase induces angiogenesis to reduce the hypoxic state and boost blood flow to tumor tissues for increasing PDT efficacy [93].

Another strategy to boost oxygen concentration in tumors is encapsulating PS and hemoglobin that can carry oxygen in the blood [94, 95]. O_2 can be produced by catalyzing the hydrogen peroxide in the TME at the tumor site Scientists have focused on catalase and enzyme-functional nanoparticles and employed them to address this issue. A targeted nanoparticle with PS and catalase was created by Chen et al. The catalase in the nanoparticle catalyzed H_2O_2 to create oxygen as it entered cells, reducing hypoxia and considerably enhanced the effectiveness of PDT [96]. At an acidic pH, manganese dioxide (MnO_2) nanoparticles can create oxygen through $MnO_2 + H_2O_2 + 2\ H + Mn^{2+} + 2H_2O + O_2$. These PS-loaded nanoparticles improved the tumor-killing efficacy [97, 98].

For PDT, nanoparticles made of perfluorocarbon, CaO_2, and carbon nitride (C_3N_4), for instance, have been created [99–101]. It is impossible to disregard the various issues that continue to exist, including toxicity, non-selectivity, inadequate O_2-carrying capacity, and ineffective administration. PDT primarily induces tumor cells' apoptosis, autophagy, and necrosis in treating cancer by producing singlet oxygen [102]. PDT has favorable anticancer effects, just like PTT. For instance, co-loading doxorubicin (DOX) and hematoporphyrin in nanoparticles can roughly 12-fold boost the sensitivity of chemotherapeutic medicines [103]. The effectiveness of chemo-PDT based on the silica-nanoparticles encapsulating with chlorin e6 and Pt co-delivery was increased 47-fold compared to free Pt exposure [104]. Li and coworkers showed that PDT mediated with PS-loaded could overcome breast cancer treatment resistance [105]. Numerous investigations have demonstrated that chemo-resistance is caused by hypoxia [106, 107]. Therefore, enhanced PDT efficacy and overcoming chemo-resistance benefit oxygen self-enriched nanoparticles [108].

4.1 Immune Checkpoint Inhibition in Conjunction with PDT

By rectifying the negative regulation between immune and tumor cells, immune checkpoint blocked (ICB) treatment enhances PDT antitumor immunological response. Following PDT treatment, there is an increase in Treg infiltration and overexpression of PD-L1 that prevents immune cells like T lymphocytes from destroying tumors [109]. So, it makes sense to combine PDT with ICB. PDT and CTLA-4 inhibition were used in a therapeutic system by Xu et al. With the use of adjuvants, this method dramatically enhances DC cell activation during PDT and demonstrates potent antitumor immunity to stop the spread of local and distant cancers. Additionally, the developed immunological memory cells can resist the recurrence of malignancies for a considerable time [67]. He and colleagues constructed core-shell nanostructures to administer the drugs oxaliplatin and PS. Tumor cells were immediately eliminated at the treatment location by the subsequent chemotherapy and PDT. They increased the concentrations of TAAs and tumor nanovaccines to trigger an immediate immune response. Combining anti-PD-L1 treatments can significantly boost survival and the efficacy of untreated distant cancers [68].

Table 1 offers more information on the combined treatments. Research interest in tumor immunotherapy using macrophages has grown recently. By suppressing the CD47/SIRP signal, the anti-CD47 can alleviate macrophage immune suppression and have anticancer effects [61]. Leukemia, breast cancer, and other malignant disorders can all be effectively treated with this antibody [110–112]. However, due to the potential adverse effects of the anti-CD47 antibody, no studies have examined PTT or PDT in combination with the anti-CD47 antibody. Therefore, it is crucial to close this research gap.

5 Multifunctional Nanoparticles for PDT/PTT

Phototherapy, specifically PTT and PDT, exhibits significant potential in the biomedical domain owing to its ability to achieve precise spatiotemporal control and noninvasive characteristics [113]. Despite light energy utilization in both processes, PTT and PDT exhibit distinct characteristics. PTT agents can capture and transform light energy into thermal energy, which can be utilized to induce hyperthermia and subsequently eliminate cancer cells [4]. On the other hand, it should be noted that in PDT, the photosensitizer is responsible for light absorption, leading to the generation of cytotoxic reactive oxygen species within cancer cells, provided oxygen is present [114]. Numerous strategies have been suggested in the literature to enhance PTT efficiency and improve PDT outcomes. These strategies include increasing the cumulative dosage of the tumor area, optimizing the laser dosage, guiding the treatment using imaging techniques, enhancing the photothermal conversion efficiency, selecting appropriate photosensitizers, utilizing indirect excitation methods, externally supplying oxygen, and other related approaches [115]. In recent studies, researchers have provided evidence that combining multiple phototherapy techniques has improved effectiveness against cancer cells compared to using PTT or PDT alone. This is particularly evident in the case of the synergistic combination of PTT and PDT [116]. Zhang et al. developed a novel class of porphyrin derivatives coupled with graphene quantum dots. These derivatives could generate $^1O_2$ upon exposure to a 635 nm laser. Additionally, they exhibited a remarkable photothermal effect, achieving a photothermal conversion efficiency of 25.58% when irradiated with a 980 nm laser [117]. Guo et al. developed a drug delivery system using black phosphorus that exhibited responsiveness to changes in pH and light. The system enabled controlled drug release, $^1O_2$ formation upon exposure to a 660 nm laser, and photothermal activity when subjected to an 808 nm laser [118]. Zhang et al. presented the findings on synthesizing biocompatible copper ferrite nanospheres. These nanospheres exhibited an increased formation of ROS when exposed to a 650 nm laser, which was attributed to both direct electron transfer and photo-enhanced Fenton reaction.

Additionally, the nanospheres demonstrated a high efficiency in converting light into heat when exposed to an 808 nm laser. While there have been advancements in synergistic antitumor efficacy, utilizing two lasers presents operational convenience and financial burden challenges. Several research have attempted to employ a combination of phototherapy using a single laser [119]. Yang et al. presented a therapeutic nanoplatform called IONCs@Ce6-DOX/PCM. This nanoplatform involved the incorporation of the photosensitizer chlorin e6 into amine-functionalized iron oxide nanocrystals. The researchers demonstrated that this nanoplatform exhibited enhanced treatment efficacy when exposed to a single 650 nm laser, thereby highlighting its potential for synergistic therapy [120]. Xia et al. conducted a study in which they selected photosensitizers, specifically indocyanine green, and modified them on the Au/MoS2 hybrid through hydrophobic interactions and π–π stacking. By employing a single 808-nm laser activation, they proposed a strategy known as simultaneous PDT and synergistic PTT. This approach effectively reduces the duration of treatment and achieves a high therapeutic index [121]. The combination of photosensitizers and PTT agents has demonstrated remarkable efficacy in inhibiting tumor growth when subjected to laser irradiation. However, a new issue has arisen. The effectiveness of photosensitizer-induced PDT is significantly hindered by the limited availability of oxygen in tumor regions despite the appropriate selection of a photosensitizer. Therefore, it is crucial to explore other methods for addressing these issues. The efficacy of free radical initiators in generating free radicals via thermal breakdown has been experimentally confirmed in the context of free radical polymerization [122]. The initial discovery of this oxygen-independent free radical as a potential agent for PDT in eliminating cancer cells. Subsequently, Xianzheng Zhang et al. conducted further investigations to elucidate the mechanism by which this radical induces cell death in tumor cells under various conditions and its potential applicability in treating hypoxic malignancies [123]. Therefore, using this particular free radical initiator in PDT to overcome malignancies has demonstrated promising prospects in cancer treatment. The formation rate of free radicals in the initiator breakdown process depends on temperature conditions [124]. PTT agents can facilitate the provision of thermal energy through light irradiation. Notably, a single laser can fulfill the requirements of combined therapy, effectively circumventing any issues associated with using lasers. Hyperthermia is essential to ensure the prompt production of an adequate quantity of free radicals in PDT and to induce the photothermal effect in PTT for tumor treatment. In addition, imaging techniques, particularly CT imaging, play a pivotal role in the guidance of phototherapy treatment. Regrettably, the effectiveness of diagnostic agents is sometimes hindered by limited X-ray attenuation coefficients [125]. In summary, a suitable PDT and PTT carrier should satisfy the following requirements: (1) a substantial carrying capacity to accommodate an adequate amount of initiators; (2) a significant photothermal conversion efficiency to generate hyperthermia and trigger the production of free radicals; and (3) a strong imaging capability to accurately identify

the tumor site. The conditions mentioned above are effectively fulfilled by hollow bismuth selenide nanoparticles, as reported by Rong Chen et al. and Miao Yu et al. These nanoparticles exhibit a high X-ray attenuation coefficient, ample loading capacity, and excellent photothermal conversion performance. Additionally, it has various other benefits, including cost-effectiveness, ease of synthesis, and compatibility with biological systems [126, 127].

6 Challenge of PTT/PDT in Clinical Applications

Nevertheless, despite the advantages above, obstacles still hinder the complete realization of the synergistic potential of phototherapy and cancer immunotherapy. A significant obstacle arises from NIR light's constrained tissue penetration depth when targeting tumors at considerable depths within the body, such as breast cancers. Consequently, phototherapy is primarily restricted to superficial tissues, with PDT occasionally being a therapeutic option for certain skin carcinomas. Currently, several new alternatives have the potential to offer advantages to counterbalance this limitation. Despite its general impermeability, it is acknowledged that a minor fraction of NIR light has the potential to penetrate deeper layers of tissues [128]. Consequently, this prompted numerous researchers to devise innovative methods for enhancing current PTT agents' thermal efficiency and stability. Moon et al. conducted a study in which they implemented an additional polydopamine coating on gold nanoparticles, resulting in enhanced and prolonged absorption capabilities. Further investigation in this field will inevitably improve the repertoire of phototherapy agents, potentially leading to the discovery of a highly successful agent [129]. Kobayashi et al. demonstrated the potential for improvisation in the delivery of the light source by combining exterior and interstitial NIR light exposure. This enhancement increased effectiveness compared to using only an external NIR light source [130]. In addition, our research team and other scholars have explored the potential for enhancing penetration depth by utilizing photothermal compounds that can effectively absorb near-infrared light in the second biological window (1000–1700 nm). It is noteworthy to emphasize that while heavy metal nanoparticles are generally more effective as agents, careful consideration should be taken when choosing them due to their tendency to accumulate in tissues over an extended period. There are lingering uncertainties regarding the safety and toxicity characteristics of these substances. The phototherapy agent targeting efficacy can be enhanced by employing antibody-drug conjugates, leading to augmented accumulation within tumor tissue or remaining tumor cells [131, 132]. Finally, oxygen availability poses a significant barrier in PDT, as generating an adequate amount of ROS is crucial to eliminating tumor cells effectively. Lin et al. employed a novel approach to address the issue of hypoxia, utilizing a metal-organic framework that facilitated a cascade of events leading to the conversion of intracellular H_2O_2 into ROS. In recent studies, scientists have successfully created hybrid core-shell semiconducting nanoparticles with the inclusion of MnO_2 sheets. These nanoparticles have demonstrated the ability to enhance O_2 evolution, specifically within hypoxic solid tumors. The review elucidates that integrating immune checkpoint immunotherapy with phototherapy holds significant potential for improving cancer prognosis. The outstanding matter pertains to identifying immunological checkpoints that improve immunosuppression regulation and effectiveness [70, 133]. A potential immunological checkpoint involves targeting CD47, a receptor protein associated with integrins that is prominently expressed on the cell membrane of diverse cancer cells. The interaction between CD47 and anti-CD47 disrupts the binding between CD47 and SIRP-alpha on macrophages and dendritic cells. This disruption reverses the "don't eat me" signal, enhancing anticancer activity. Moon et al. revealed an intriguing alternate approach, including non-immunotherapeutic methods to induce an immunotherapeutic response. In addition to utilizing immunotherapeutic techniques, it is noteworthy to consider integrating alternative phototherapeutic methods that may synergistically complement immunotherapy, hence presenting the potential for achieving complete restoration of health [70, 134].

7 Conclusion and Perspectives

In conclusion, nanomaterial-based phototherapy can stimulate the immune system through the following pathways, in addition to eradicating tumor cells directly and reversing treatment resistance. After PTT or PDT kills the tumor cells, the body's immune system is stimulated by releasing tumor-associated antigens and cell debris. This results in the activation and reorganization of immune effector cells (like NK cells, DCs, T lymphocytes, and macrophages), as well as the expression and secretion of cytokines. Immune adjuvants and checkpoint inhibitors can treat both primary and metastatic cancers while improving antitumor immunity. Despite substantial research into nanomaterial-based photo/immunotherapy, these studies are still in the laboratory and are currently dealing with several difficulties. For instance, it is essential to consider the targeting and safety of nanomaterials-based PTT and PDT and their potential use in metastatic and deep cancers.

Additionally, PTT and PDT-induced immune responses in vivo are complicated, and it is yet unclear exactly how they manifest and work. It's also important to consider the

strength and controllability of immune responses. Therefore, more research into photothermal and photodynamic immunotherapy using nanoparticles is required.

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References

1. Mohammadian, F., Pilehvar-Soltanahmadi, Y., Alipour, S., Dadashpour, M., & Zarghami, N. (2017). Chrysin alters microRNAs expression levels in gastric cancer cells: Possible molecular mechanism. *Drug Research, 67*(09), 509–514.
2. Marofi, F., Abdul-Rasheed, O. F., Rahman, H. S., Budi, H. S., Jalil, A. T., Yumashev, A. V., Hassanzadeh, A., Yazdanifar, M., Motavalli, R., & Chartrand, M. S. (2021). CAR-NK cell in cancer immunotherapy; A promising frontier. *Cancer Science, 112*(9), 3427–3436.
3. Achmad, H., Ibrahim, Y. S., Al-Taee, M. M., Gabr, G. A., Riaz, M. W., Alshahrani, S. H., Ramírez-Coronel, A. A., Jalil, A. T., Budi, H. S., & Sawitri, W. (2022). Nanovaccines in cancer immunotherapy: Focusing on dendritic cell targeting. *International Immunopharmacology, 113*, 109434.
4. Dercle, L., Ammari, S., Seban, R.-D., Schwartz, L. H., Houot, R., Labaied, N., Mokrane, F.-Z., Lazarovici, J., Danu, A., & Marabelle, A. (2018). Kinetics and nadir of responses to immune checkpoint blockade by anti-PD1 in patients with classical Hodgkin lymphoma. *European Journal of Cancer, 91*, 136–144.
5. Dirix, L. Y., Takacs, I., Jerusalem, G., Nikolinakos, P., Arkenau, H.-T., Forero-Torres, A., Boccia, R., Lippman, M. E., Somer, R., & Smakal, M. (2018). Avelumab, an anti-PD-L1 antibody, in patients with locally advanced or metastatic breast cancer: A phase 1b JAVELIN solid tumor study. *Breast Cancer Research and Treatment, 167*(3), 671–686.
6. Sakamuri, D., Glitza, I. C., Betancourt Cuellar, S. L., Subbiah, V., Fu, S., Tsimberidou, A. M., Wheler, J. J., Hong, D. S., Naing, A., & Falchook, G. S. (2018). Phase I dose-escalation study of anti–CTLA-4 antibody ipilimumab and lenalidomide in patients with advanced cancersipilimumab and lenalidomide in advanced malignancies. *Molecular Cancer Therapeutics, 17*(3), 671–676.
7. Mao, L., Xiao, Y., Yang, Q.-C., Yang, S.-C., Yang, L.-L., & Sun, Z.-J. (2021). TIGIT/CD155 blockade enhances anti-PD-L1 therapy in head and neck squamous cell carcinoma by targeting myeloid-derived suppressor cells. *Oral Oncology, 121*, 105472.
8. Ray, A., Das, D. S., Song, Y., Hideshima, T., Tai, Y.-T., Chauhan, D., & Anderson, K. C. (2018). Combination of a novel HDAC6 inhibitor ACY-241 and anti-PD-L1 antibody enhances anti-tumor immunity and cytotoxicity in multiple myeloma. *Leukemia, 32*(3), 843–846.
9. Wen, X., Zeng, X., Cheng, X., Zeng, X., Liu, J., Zhang, Y., Li, Y., Chen, H., Huang, J., & Guo, Z. (2022). PD-L1-Targeted radionuclide therapy combined with αPD-L1 antibody immunotherapy synergistically improves the antitumor effect. *Molecular Pharmaceutics*. https://doi.org/10.1021/acs.molpharmaceut.2c00281
10. Li, Y., Yang, Z., Jalil, A. T., Saleh, M. M., & Wu, B. (2023). In vivo and in vitro biocompatibility study of CuS nanoparticles: Photosensitizer for glioblastoma photothermal therapy. *Applied Biochemistry and Biotechnology*. https://doi.org/10.1007/s12010-023-04313-3
11. Kaufman, H. L., Russell, J., Hamid, O., Bhatia, S., Terheyden, P., D'Angelo, S. P., Shih, K. C., Lebbé, C., Linette, G. P., & Milella, M. (2016). Avelumab in patients with chemotherapy-refractory metastatic merkel cell carcinoma: A multicentre, single-group, open-label, phase 2 trial. *The Lancet Oncology, 17*(10), 1374–1385.
12. Sade-Feldman, M., Jiao, Y. J., Chen, J. H., Rooney, M. S., Barzily-Rokni, M., Eliane, J.-P., Bjorgaard, S. L., Hammond, M. R., Vitzthum, H., & Blackmon, S. M. (2017). Resistance to checkpoint blockade therapy through inactivation of antigen presentation. *Nature Communications, 8*(1), 1–11.
13. Pollack, M., Betof, A., Dearden, H., Rapazzo, K., Valentine, I., Brohl, A., Ancell, K., Long, G., Menzies, A., & Eroglu, Z. (2018). Safety of resuming anti-PD-1 in patients with immune-related adverse events (irAEs) during combined anti-CTLA-4 and anti-PD1 in metastatic melanoma. *Annals of Oncology, 29*(1), 250–255.
14. Costa, R., Costa, R. B., Talamantes, S. M., Helenoswki, I., Carneiro, B. A., Chae, Y. K., Gradishar, W. J., Kurzrock, R., & Giles, F. J. (2017). Analyses of selected safety endpoints in phase 1 and late-phase clinical trials of anti-PD-1 and PD-L1 inhibitors: Prediction of immune-related toxicities. *Oncotarget, 8*(40), 67782.
15. Johnson, D. B., Balko, J. M., Compton, M. L., Chalkias, S., Gorham, J., Xu, Y., Hicks, M., Puzanov, I., Alexander, M. R., & Bloomer, T. L. (2016). Fulminant myocarditis with combination immune checkpoint blockade. *New England Journal of Medicine, 375*(18), 1749–1755.
16. Shaban SA, Al-Rahim AM, Suleiman AA. ALU repeat as potential molecular marker in the detection and prognosis of different cancer types: A systematic review. Molecular and Clinical Oncology. 2022 Apr 1;16(4):1-9.
17. Kudo, M. (2022). Atezolizumab plus bevacizumab followed by curative conversion (ABC conversion) in patients with unresectable, TACE-unsuitable intermediate-stage hepatocellular carcinoma. *Liver Cancer, 11*(5), 399–406.
18. Takaki, H., Cornelis, F., Kako, Y., Kobayashi, K., Kamikonya, N., & Yamakado, K. (2017). Thermal ablation and immunomodulation: From preclinical experiments to clinical trials. *Diagnostic and Interventional Imaging, 98*(9), 651–659.
19. Wu, W., Pu, Y., & Shi, J. (2022). Nanomedicine-enabled chemotherapy-based synergetic cancer treatments. *Journal of Nanobiotechnology, 20*(1), 1–21.
20. Pakravan, A., Azizi, M., Rahimi, F., Bani, F., Mahmoudzadeh, F., Salehi, R., & Mahkam, M. (2021). Comparative effect of thermo/pH-responsive polymer-coated gold nanocages and hollow nanostars on chemo-photothermal therapy of breast cancer cells. *Cancer Nanotechnology, 12*(1), 1–26.
21. Ali, M. R., Ali, H. R., Rankin, C. R., & El-Sayed, M. A. (2016). Targeting heat shock protein 70 using gold nanorods

enhances cancer cell apoptosis in low dose plasmonic photothermal therapy. *Biomaterials, 102*, 1–8.
22. Talaei, S., Mellatyar, H., Pilehvar-Soltanahmadi, Y., Asadi, A., Akbarzadeh, A., & Zarghami, N. (2019). 17-Allylamino-17-demethoxygeldanamycin loaded PCL/PEG nanofibrous scaffold for effective growth inhibition of T47D breast cancer cells. *Journal of Drug Delivery Science and Technology, 49*, 162–168.
23. Wang, S., Li, L., Ning, X., Xue, P., & Liu, Y. (2019). pH-activated heat shock protein inhibition and radical generation enhanced NIR luminescence imaging-guided photothermal tumour ablation. *International Journal of Pharmaceutics, 566*, 40–45.
24. Guo, Z., Liu, Y., Cheng, X., Wang, D., Guo, S., Jia, M., Ma, K., Cui, C., Wang, L., & Zhou, H. (2020). Versatile biomimetic cantharidin-tellurium nanoparticles enhance photothermal therapy by inhibiting the heat shock response for combined tumor therapy. *Acta Biomaterialia, 110*, 208–220.
25. Wang, S., Tian, Y., Tian, W., Sun, J., Zhao, S., Liu, Y., Wang, C., Tang, Y., Ma, X., & Teng, Z. (2016). Selectively sensitizing malignant cells to photothermal therapy using a CD44-targeting heat shock protein 72 depletion nanosystem. *ACS Nano, 10*(9), 8578–8590.
26. Xu, H., Ito, T., Tawada, A., Maeda, H., Yamanokuchi, H., Isahara, K., Yoshida, K., Uchiyama, Y., & Asari, A. (2002). Effect of hyaluronan oligosaccharides on the expression of heat shock protein 72. *Journal of Biological Chemistry, 277*(19), 17308–17314.
27. Qiao, L., Mei, Z., Yang, Z., Li, X., Cai, H., & Liu, W. (2016). ALA-PDT inhibits proliferation and promotes apoptosis of SCC cells through STAT3 signal pathway. *Photodiagnosis and Photodynamic Therapy, 14*, 66–73.
28. Edmonds, C., Hagan, S., Gallagher-Colombo, S. M., Busch, T. M., & Cengel, K. A. (2012). Photodynamic therapy activated signaling from epidermal growth factor receptor and STAT3: Targeting survival pathways to increase PDT efficacy in ovarian and lung cancer. *Cancer Biology & Therapy, 13*(14), 1463–1470.
29. Wan, S.-S., Zeng, J.-Y., Cheng, H., & Zhang, X.-Z. (2018). ROS-induced NO generation for gas therapy and sensitizing photodynamic therapy of tumor. *Biomaterials, 185*, 51–62.
30. Srivatsan, A., Wang, Y., Joshi, P., Sajjad, M., Chen, Y., Liu, C., Thankppan, K., Missert, J. R., Tracy, E., & Morgan, J. (2011). In vitro cellular uptake and dimerization of signal transducer and activator of transcription-3 (STAT3) identify the photosensitizing and imaging-potential of isomeric photosensitizers derived from chlorophyll-a and bacteriochlorophyll-a. *Journal of Medicinal Chemistry, 54*(19), 6859–6873.
31. Gibault, F., Corvaisier, M., Bailly, F., Huet, G., Melnyk, P., & Cotelle, P. (2016). Non-photoinduced biological properties of verteporfin. *Current Medicinal Chemistry, 23*(11), 1171–1184.
32. Li, Y., Li, X., Doughty, A., West, C., Wang, L., Zhou, F., Nordquist, R. E., & Chen, W. R. (2019). Phototherapy using immunologically modified carbon nanotubes to potentiate checkpoint blockade for metastatic breast cancer. *Nanomedicine: Nanotechnology, Biology and Medicine, 18*, 44–53.
33. Domvri, K., Petanidis, S., Anestakis, D., Porpodis, K., Bai, C., Zarogoulidis, P., Freitag, L., Hohenforst-Schmidt, W., & Katopodi, T. (2020). Dual photothermal MDSCs-targeted immunotherapy inhibits lung immunosuppressive metastasis by enhancing T-cell recruitment. *Nanoscale, 12*(13), 7051–7062.
34. Saneja, A., Kumar, R., Arora, D., Kumar, S., Panda, A. K., & Jaglan, S. (2018). Recent advances in near-infrared light-responsive nanocarriers for cancer therapy. *Drug Discovery Today, 23*(5), 1115–1125.
35. Al-Hetty, H. R. A. K., Jalil, A. T., Alghazali, M. W., fadel, H. A., Ahmed, O. S., Abosaooda, M., & Ali, M. (2023). Nanomaterials for combination cancer photothermal therapy. *Emergent Materials*. https://doi.org/10.1007/s42247-023-00464-5
36. Zhu, X., Zhang, Y., Huang, H., Zhang, H., Hou, L., & Zhang, Z. (2017). Folic acid-modified and functionalized CuS nanocrystal-based nanoparticles for combined tumor chemo-and photothermal therapy. *Journal of Drug Targeting, 25*(5), 425–435.
37. Han, Z., Gao, M., Wang, Z., Peng, L., Zhao, Y., & Sun, L. (2022). pH/NIR-responsive nanocarriers based on mesoporous polydopamine encapsulated gold nanorods for drug delivery and thermochemotherapy. *Journal of Drug Delivery Science and Technology, 75*, 103610.
38. Ju, Y., Zhang, H., Yu, J., Tong, S., Tian, N., Wang, Z., Wang, X., Su, X., Chu, X., & Lin, J. (2017). Monodisperse Au–Fe2C Janus nanoparticles: An attractive multifunctional material for triple-modal imaging-guided tumor photothermal therapy. *ACS Nano, 11*(9), 9239–9248.
39. Song, S., Shen, H., Yang, T., Wang, L., Fu, H., Chen, H., & Zhang, Z. (2017). Indocyanine green loaded magnetic carbon nanoparticles for near infrared fluorescence/magnetic resonance dual-modal imaging and photothermal therapy of tumor. *ACS Applied Materials & Interfaces, 9*(11), 9484–9495.
40. Hu, Y., Chi, C., Wang, S., Wang, L., Liang, P., Liu, F., Shang, W., Wang, W., Zhang, F., & Li, S. (2017). A comparative study of clinical intervention and interventional photothermal therapy for pancreatic cancer. *Advanced Materials, 29*(33), 1700448.
41. Wei, W., Zarghami, N., Abasi, M., Ertas, Y. N., & Pilehvar, Y. (2022). Implantable magnetic nanofibers with ON–OFF switchable release of curcumin for possible local hyperthermic chemotherapy of melanoma. *Journal of Biomedical Materials Research Part A, 110*(4), 851–860.
42. Valizadeh, A., Asghari, S., Abbaspoor, S., Jafari, A., Raeisi, M., & Pilehvar, Y. (2023). Implantable smart hyperthermia nanofibers for cancer therapy: Challenges and opportunities. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*. https://doi.org/10.1002/wnan.1909
43. Jung, H. S., Han, J., Lee, J.-H., Lee, J. H., Choi, J.-M., Kweon, H.-S., Han, J. H., Kim, J.-H., Byun, K. M., & Jung, J. H. (2015). Enhanced NIR radiation-triggered hyperthermia by mitochondrial targeting. *Journal of the American Chemical Society, 137*(8), 3017–3023.
44. Jung, H. S., Lee, J.-H., Kim, K., Koo, S., Verwilst, P., Sessler, J. L., Kang, C., & Kim, J. S. (2017). A mitochondria-targeted cryptocyanine-based photothermogenic photosensitizer. *Journal of the American Chemical Society, 139*(29), 9972–9978.
45. Pan, L., Liu, J., & Shi, J. (2017). Nuclear-targeting gold nanorods for extremely low NIR activated photothermal therapy. *ACS Applied Materials & Interfaces, 9*(19), 15952–15961.
46. Belity, T., Horowitz, M., Hoffman, J. R., Epstein, Y., Bruchim, Y., Todder, D., & Cohen, H. (2022). Heat-stress preconditioning attenuates behavioral responses to psychological stress: The Role of HSP-70 in modulating stress responses. *International Journal of Molecular Sciences, 23*(8), 4129.
47. Calderwood, S. K., & Gong, J. (2016). Heat shock proteins promote cancer: It's a protection racket. *Trends in Biochemical Sciences, 41*(4), 311–323.
48. Chen, W.-H., Luo, G.-F., Lei, Q., Hong, S., Qiu, W.-X., Liu, L.-H., Cheng, S.-X., & Zhang, X.-Z. (2017). Overcoming the heat endurance of tumor cells by interfering with the anaerobic glycolysis metabolism for improved photothermal therapy. *ACS Nano, 11*(2), 1419–1431.
49. Yang, Y., Zhu, W., Dong, Z., Chao, Y., Xu, L., Chen, M., & Liu, Z. (2017). 1D coordination polymer nanofibers for low-temperature photothermal therapy. *Advanced Materials, 29*(40), 1703588.
50. Wang, Z., Li, S., Zhang, M., Ma, Y., Liu, Y., Gao, W., Zhang, J., & Gu, Y. (2017). Laser-triggered small interfering RNA

releasing gold nanoshells against heat shock protein for sensitized photothermal therapy. *Advanced Science, 4*(2), 1600327.
51. Yang, L., Tseng, Y.-T., Suo, G., Chen, L., Yu, J., Chiu, W.-J., Huang, C.-C., & Lin, C.-H. (2015). Photothermal therapeutic response of cancer cells to aptamer–gold nanoparticle-hybridized graphene oxide under NIR illumination. *ACS Applied Materials & Interfaces, 7*(9), 5097–5106.
52. Chatterjee, M., Andrulis, M., Stühmer, T., Müller, E., Hofmann, C., Steinbrunn, T., Heimberger, T., Schraud, H., Kressmann, S., & Einsele, H. (2013). The PI3K/Akt signaling pathway regulates the expression of Hsp70, which critically contributes to Hsp90-chaperone function and tumor cell survival in multiple myeloma. *Haematologica, 98*(7), 1132.
53. Wang, T., Wang, D., Yu, H., Wang, M., Liu, J., Feng, B., Zhou, F., Yin, Q., Zhang, Z., & Huang, Y. (2016). Intracellularly acid-switchable multifunctional micelles for combinational photo/chemotherapy of the drug-resistant tumor. *ACS Nano, 10*(3), 3496–3508.
54. Fletcher, J. I., Williams, R. T., Henderson, M. J., Norris, M. D., & Haber, M. (2016). ABC transporters as mediators of drug resistance and contributors to cancer cell biology. *Drug Resistance Updates, 26*, 1–9.
55. Li, Y., Deng, Y., Tian, X., Ke, H., Guo, M., Zhu, A., Yang, T., Guo, Z., Ge, Z., & Yang, X. (2015). Multipronged design of light-triggered nanoparticles to overcome cisplatin resistance for efficient ablation of resistant tumor. *ACS Nano, 9*(10), 9626–9637.
56. Wang, L., Lin, X., Wang, J., Hu, Z., Ji, Y., Hou, S., Zhao, Y., Wu, X., & Chen, C. (2014). Novel insights into combating cancer chemotherapy resistance using a plasmonic nanocarrier: Enhancing drug sensitiveness and accumulation simultaneously with localized mild photothermal stimulus of femtosecond pulsed laser. *Advanced Functional Materials., 24*(27), 4229–4239.
57. Wang, L., Sun, Q., Wang, X., Wen, T., Yin, J.-J., Wang, P., Bai, R., Zhang, X.-Q., Zhang, L.-H., & Lu, A.-H. (2015). Using hollow carbon nanospheres as a light-induced free radical generator to overcome chemotherapy resistance. *Journal of the American Chemical Society, 137*(5), 1947–1955.
58. Fay, B. L., Melamed, J. R., & Day, E. S. (2015). Nanoshell-mediated photothermal therapy can enhance chemotherapy in inflammatory breast cancer cells. *International Journal of Nanomedicine, 10*, 6931.
59. DeMichele, A., Yee, D., & Esserman, L. (2017). Mechanisms of resistance to neoadjuvant chemotherapy in breast cancer. *New England Journal of Medicine, 377*(23), 2287–2289.
60. Wang, C., Xu, L., Liang, C., Xiang, J., Peng, R., & Liu, Z. (2014). Immunological responses triggered by photothermal therapy with carbon nanotubes in combination with anti-CTLA-4 therapy to inhibit cancer metastasis. *Advanced Materials, 26*(48), 8154–8162.
61. Zhao, X. W., van Beek, E. M., Schornagel, K., Van der Maaden, H., Van Houdt, M., Otten, M. A., Finetti, P., Van Egmond, M., Matozaki, T., & Kraal, G. (2011). CD47–signal regulatory protein-α (SIRPα) interactions form a barrier for antibody-mediated tumor cell destruction. *Proceedings of the National Academy of Sciences, 108*(45), 18342–18347.
62. Chen, Q., Xu, L., Liang, C., Wang, C., Peng, R., & Liu, Z. (2016). Photothermal therapy with immune-adjuvant nanoparticles together with checkpoint blockade for effective cancer immunotherapy. *Nature Communications, 7*(1), 1–13.
63. Liu, Y., Maccarini, P., Palmer, G. M., Etienne, W., Zhao, Y., Lee, C.-T., Ma, X., Inman, B. A., & Vo-Dinh, T. (2017). Synergistic immuno photothermal nanotherapy (SYMPHONY) for the treatment of unresectable and metastatic cancers. *Scientific Reports, 7*(1), 1–6.
64. Sharma, P., & Allison, J. P. (2015). The future of immune checkpoint therapy. *Science, 348*(6230), 56–61.
65. Long, G. V., Atkinson, V., Lo, S., Sandhu, S., Guminski, A. D., Brown, M. P., Wilmott, J. S., Edwards, J., Gonzalez, M., & Scolyer, R. A. (2018). Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: A multicentre randomised phase 2 study. *The Lancet Oncology, 19*(5), 672–681.
66. D'Angelo, S. P., Mahoney, M. R., Van Tine, B. A., Atkins, J., Milhem, M. M., Jahagirdar, B. N., Antonescu, C. R., Horvath, E., Tap, W. D., & Schwartz, G. K. (2018). Nivolumab with or without ipilimumab treatment for metastatic sarcoma (Alliance A091401): Two open-label, non-comparative, randomised, phase 2 trials. *The Lancet Oncology, 19*(3), 416–426.
67. Hellmann, M. D., Callahan, M. K., Awad, M. M., Calvo, E., Ascierto, P. A., Atmaca, A., Rizvi, N. A., Hirsch, F. R., Selvaggi, G., & Szustakowski, J. D. (2019). Tumor mutational burden and efficacy of nivolumab monotherapy and in combination with ipilimumab in small-cell lung cancer. *Cancer Cell, 35*(2), 329.
68. Wolchok, J. D., Chiarion-Sileni, V., Gonzalez, R., Grob, J.-J., Rutkowski, P., Lao, C. D., Cowey, C. L., Schadendorf, D., Wagstaff, J., & Dummer, R. (2022). Long-term outcomes with nivolumab plus ipilimumab or nivolumab alone versus ipilimumab in patients with advanced melanoma. *Journal of Clinical Oncology, 40*(2), 127–137.
69. Wolchok, J. D., Chiarion-Sileni, V., Gonzalez, R., Rutkowski, P., Grob, J.-J., Cowey, C. L., Lao, C. D., Wagstaff, J., Schadendorf, D., & Ferrucci, P. F. (2017). Overall survival with combined nivolumab and ipilimumab in advanced melanoma. *New England Journal of Medicine, 377*(14), 1345–1356.
70. Park, W., Cho, S., Han, J., Shin, H., Na, K., Lee, B., & Kim, D.-H. (2018). Advanced smart-photosensitizers for more effective cancer treatment. *Biomaterials Science, 6*(1), 79–90.
71. Tsai, W.-H., Yu, K.-H., Huang, Y.-C., & Lee, C.-I. (2018). EGFR-targeted photodynamic therapy by curcumin-encapsulated chitosan/TPP nanoparticles. *International Journal of Nanomedicine, 13*, 903.
72. Dos Santos, A. F., Terra, L. F., Wailemann, R. A., Oliveira, T. C., Gomes, Vd. M., Mineiro, M. F., Meotti, F. C., Bruni-Cardoso, A., Baptista, M. S., & Labriola, L. (2017). Methylene blue photodynamic therapy induces selective and massive cell death in human breast cancer cells. *BMC Cancer, 17*(1), 1–15.
73. Lopez, R. F. V., Lange, N., Guy, R., & Bentley, M. V. L. B. (2004). Photodynamic therapy of skin cancer: Controlled drug delivery of 5-ALA and its esters. *Advanced Drug Delivery Reviews, 56*(1), 77–94.
74. Moghissi, K., & Dixon, K. (2003). Is bronchoscopic photodynamic therapy a therapeutic option in lung cancer? *European Respiratory Journal, 22*(3), 535–541.
75. Zhang, Y., Wang, F., Liu, C., Wang, Z., Kang, L., Huang, Y., Dong, K., Ren, J., & Qu, X. (2018). Nanozyme decorated metal-organic frameworks for enhanced photodynamic therapy. *ACS Nano, 12*(1), 651–661.
76. Chizenga, E. P., & Abrahamse, H. (2020). Nanotechnology in modern photodynamic therapy of cancer: A review of cellular resistance patterns affecting the therapeutic response. *Pharmaceutics, 12*(7), 632.
77. Kato, T., Jin, C. S., Ujiie, H., Lee, D., Fujino, K., Wada, H., Hu, H.-p, Weersink, R. A., Chen, J., & Kaji, M. (2017). Nanoparticle targeted folate receptor 1-enhanced photodynamic therapy for lung cancer. *Lung Cancer, 113*, 59–68.
78. Wang, C., Cheng, L., & Liu, Z. (2013). Upconversion nanoparticles for photodynamic therapy and other cancer therapeutics. *Theranostics, 3*(5), 317.
79. Akbari, T., Pourhajibagher, M., Hosseini, F., Chiniforush, N., Gholibegloo, E., Khoobi, M., Shahabi, S., & Bahador, A. (2017). The effect of indocyanine green loaded on a novel

nano-graphene oxide for high performance of photodynamic therapy against *Enterococcus faecalis*. *Photodiagnosis and Photodynamic Therapy, 20*, 148–153.
80. Wang, K., Zhang, Y., Wang, J., Yuan, A., Sun, M., Wu, J., & Hu, Y. (2016). Self-assembled IR780-loaded transferrin nanoparticles as an imaging, targeting and PDT/PTT agent for cancer therapy. *Scientific Reports, 6*(1), 1–11.
81. Li, W., Peng, J., Tan, L., Wu, J., Shi, K., Qu, Y., Wei, X., & Qian, Z. (2016). Mild photothermal therapy/photodynamic therapy/chemotherapy of breast cancer by Lyp-1 modified Docetaxel/IR820 Co-loaded micelles. *Biomaterials, 106*, 119–133.
82. Vankayala, R., Huang, Y. K., Kalluru, P., Chiang, C. S., & Hwang, K. C. (2014). First demonstration of gold nanorods-mediated photodynamic therapeutic destruction of tumors via near infra-red light activation. *Small (Weinheim an der Bergstrasse, Germany), 10*(8), 1612–1622.
83. Gu, T., Cheng, L., Gong, F., Xu, J., Li, X., Han, G., & Liu, Z. (2018). Upconversion composite nanoparticles for tumor hypoxia modulation and enhanced near-infrared-triggered photodynamic therapy. *ACS Applied Materials & Interfaces, 10*(18), 15494–15503.
84. Gulzar, A., Xu, J., Yang, D., Xu, L., He, F., Gai, S., & Yang, P. (2020). Correction: Nano-graphene oxide-UCNP-Ce6 covalently constructed nanocomposites for NIR-mediated bioimaging and PTT/PDT combinatorial therapy. *Dalton Transactions, 49*(26), 9164–9165.
85. Li, Y., Tang, J., Pan, D.-X., Sun, L.-D., Chen, C., Liu, Y., Wang, Y.-F., Shi, S., & Yan, C.-H. (2016). A versatile imaging and therapeutic platform based on dual-band luminescent lanthanide nanoparticles toward tumor metastasis inhibition. *ACS Nano, 10*(2), 2766–2773.
86. Cheng, Y., Cheng, H., Jiang, C., Qiu, X., Wang, K., Huan, W., Yuan, A., Wu, J., & Hu, Y. (2015). Perfluorocarbon nanoparticles enhance reactive oxygen levels and tumour growth inhibition in photodynamic therapy. *Nature Communications, 6*(1), 1–8.
87. Gong, H., Chao, Y., Xiang, J., Han, X., Song, G., Feng, L., Liu, J., Yang, G., Chen, Q., & Liu, Z. (2016). Hyaluronidase to enhance nanoparticle-based photodynamic tumor therapy. *Nano Letters, 16*(4), 2512–2521.
88. Guo, X., Qu, J., Zhu, C., Li, W., Luo, L., Yang, J., Yin, X., Li, Q., Du, Y., & Chen, D. (2018). Synchronous delivery of oxygen and photosensitizer for alleviation of hypoxia tumor microenvironment and dramatically enhanced photodynamic therapy. *Drug Delivery, 25*(1), 585–599.
89. Luo, Z., Zheng, M., Zhao, P., Chen, Z., Siu, F., Gong, P., Gao, G., Sheng, Z., Zheng, C., & Ma, Y. (2016). Self-monitoring artificial red cells with sufficient oxygen supply for enhanced photodynamic therapy. *Scientific Reports, 6*(1), 1–11.
90. Chen, H., Tian, J., He, W., & Guo, Z. (2015). H2O2-activatable and O2-evolving nanoparticles for highly efficient and selective photodynamic therapy against hypoxic tumor cells. *Journal of the American Chemical Society, 137*(4), 1539–1547.
91. Peng, J., Yang, Q., Li, W., Tan, L., Xiao, Y., Chen, L., Hao, Y., & Qian, Z. (2017). Erythrocyte-membrane-coated prussian blue/manganese dioxide nanoparticles as H2O2-responsive oxygen generators to enhance cancer chemotherapy/photothermal therapy. *ACS Applied Materials & Interfaces, 9*(51), 44410–44422.
92. Gao, S., Wang, G., Qin, Z., Wang, X., Zhao, G., Ma, Q., & Zhu, L. (2017). Oxygen-generating hybrid nanoparticles to enhance fluorescent/photoacoustic/ultrasound imaging guided tumor photodynamic therapy. *Biomaterials, 112*, 324–335.
93. Zheng, D.-W., Li, B., Li, C.-X., Fan, J.-X., Lei, Q., Li, C., Xu, Z., & Zhang, X.-Z. (2016). Carbon-dot-decorated carbon nitride nanoparticles for enhanced photodynamic therapy against hypoxic tumor via water splitting. *ACS Nano, 10*(9), 8715–8722.
94. Sheng, Y., Nesbitt, H., Callan, B., Taylor, M. A., Love, M., McHale, A. P., & Callan, J. F. (2017). Oxygen generating nanoparticles for improved photodynamic therapy of hypoxic tumours. *Journal of Controlled Release, 264*, 333–340.
95. Kazaal, M., Habeeb, A. A., & Hasan, H. N. (2023). Evaluation Role of IL-13 and Eosinophils in Adult Asthmatic Patients. Journal of Biomedicine and Biochemistry, 2(2), 17-25. doi: 10.57238/jbb.2023.6940.1033
96. Skupin-Mrugalska, P., Sobotta, L., Kucinska, M., Murias, M., Mielcarek, J., & Duzgunes, N. (2014). Cellular changes, molecular pathways and the immune system following photodynamic treatment. *Current Medicinal Chemistry, 21*(35), 4059–4073.
97. Ren, Y., Wang, R., Liu, Y., Guo, H., Zhou, X., Yuan, X., Liu, C., Tian, J., Yin, H., & Wang, Y. (2014). A hematoporphyrin-based delivery system for drug resistance reversal and tumor ablation. *Biomaterials, 35*(8), 2462–2470.
98. Zhang, W., Shen, J., Su, H., Mu, G., Sun, J.-H., Tan, C.-P., Liang, X.-J., Ji, L.-N., & Mao, Z.-W. (2016). Co-delivery of cisplatin prodrug and chlorin e6 by mesoporous silica nanoparticles for chemo-photodynamic combination therapy to combat drug resistance. *ACS Applied Materials & Interfaces, 8*(21), 13332–13340.
99. Li, H., Liu, C., Zeng, Y.-P., Hao, Y.-H., Huang, J.-W., Yang, Z.-Y., & Li, R. (2016). Nanoceria-mediated drug delivery for targeted photodynamic therapy on drug-resistant breast cancer. *ACS Applied Materials & Interfaces, 8*(46), 31510–31523.
100. He, X., Wang, J., Wei, W., Shi, M., Xin, B., Zhang, T., & Shen, X. (2016). Hypoxia regulates ABCG2 activity through the activivation of ERK1/2/HIF-1α and contributes to chemoresistance in pancreatic cancer cells. *Cancer Biology & Therapy, 17*(2), 188–198.
101. Rosa, P., Catacuzzeno, L., Sforna, L., Mangino, G., Carlomagno, S., Mincione, G., Petrozza, V., Ragona, G., Franciolini, F., & Calogero, A. (2018). BK channels blockage inhibits hypoxia-induced migration and chemoresistance to cisplatin in human glioblastoma cells. *Journal of Cellular Physiology, 233*(9), 6866–6877.
102. Yao, C., Wang, W., Wang, P., Zhao, M., Li, X., & Zhang, F. (2018). Near-infrared upconversion mesoporous cerium oxide hollow biophotocatalyst for concurrent pH-/H2O2-responsive O2-evolving synergetic cancer therapy. *Advanced Materials, 30*(7), 1704833.
103. Theodoraki, M.-N., Lorenz, K., Lotfi, R., Fuerst, D., Tsamadou, C., Jaekle, S., Mytilineos, J., Brunner, C., Theodorakis, J., & Hoffmann, T. (2017). Influence of photodynamic therapy on peripheral immune cell populations and cytokine concentrations in head and neck cancer. *Photodiagnosis and Photodynamic Therapy, 19*, 194–201.
104. Xu, J., Xu, L., Wang, C., Yang, R., Zhuang, Q., Han, X., Dong, Z., Zhu, W., Peng, R., & Liu, Z. (2017). Near-infrared-triggered photodynamic therapy with multitasking upconversion nanoparticles in combination with checkpoint blockade for immunotherapy of colorectal cancer. *ACS Nano, 11*(5), 4463–4474.
105. He, C., Duan, X., Guo, N., Chan, C., Poon, C., Weichselbaum, R. R., & Lin, W. (2016). Core-shell nanoscale coordination polymers combine chemotherapy and photodynamic therapy to potentiate checkpoint blockade cancer immunotherapy. *Nature Communications, 7*(1), 1–12.
106. Majeti, R., Chao, M. P., Alizadeh, A. A., Pang, W. W., Jaiswal, S., Gibbs, K. D., Jr., van Rooijen, N., & Weissman, I. L. (2009). CD47 is an adverse prognostic factor and therapeutic antibody target on human acute myeloid leukemia stem cells. *Cell, 138*(2), 286–299.
107. Liu, L., Zhang, L., Yang, L., Li, H., Li, R., Yu, J., Yang, L., Wei, F., Yan, C., & Sun, Q. (2017). Anti-CD47 antibody as a targeted therapeutic agent for human lung cancer and cancer stem cells. *Frontiers in Immunology, 8*, 404.

108. Kaur, S., Elkahloun, A. G., Singh, S. P., Chen, Q.-R., Meerzaman, D. M., Song, T., Manu, N., Wu, W., Mannan, P., & Garfield, S. H. (2016). A function-blocking CD47 antibody suppresses stem cell and EGF signaling in triple-negative breast cancer. *Oncotarget, 7*(9), 10133.
109. Wang, X., Zhang, J., Wang, Y., Wang, C., Xiao, J., Zhang, Q., & Cheng, Y. (2016). Multi-responsive photothermal-chemotherapy with drug-loaded melanin-like nanoparticles for synergetic tumor ablation. *Biomaterials, 81*, 114–124.
110. Fan, W., Huang, P., & Chen, X. (2016). Overcoming the Achilles' heel of photodynamic therapy. *Chemical Society Reviews, 45*(23), 6488–6519.
111. Li, X., Liu, Y., Fu, F., Cheng, M., Liu, Y., Yu, L., Wang, W., Wan, Y., & Yuan, Z. (2019). Single NIR laser-activated multifunctional nanoparticles for cascaded photothermal and oxygen-independent photodynamic therapy. *Nano-Micro Letters, 11*, 1–19.
112. You, Q., Sun, Q., Wang, J., Tan, X., Pang, X., Liu, L., Yu, M., Tan, F., & Li, N. (2017). A single-light triggered and dual-imaging guided multifunctional platform for combined photothermal and photodynamic therapy based on TD-controlled and ICG-loaded CuS@mSiO$_2$. *Nanoscale, 9*(11), 3784–3796.
113. Cao, Y., Dong, H., Yang, Z., Zhong, X., Chen, Y., Dai, W., & Zhang, X. (2017). Aptamer-conjugated graphene quantum dots/porphyrin derivative theranostic agent for intracellular cancer-related microRNA detection and fluorescence-guided photothermal/photodynamic synergetic therapy. *ACS Applied Materials & Interfaces, 9*(1), 159–166.
114. Chupradit S, Jasim SA, Bokov D, Mahmoud MZ, Roomi AB, Hachem K, Rudiansyah M, Suksatan W, Bidares R. Recent advances in biosensor devices for HER-2 cancer biomarker detection. Analytical Methods. 2022;14(13):1301-10.
115. Dai, X., Zhao, Y., Yu, Y., Chen, X., Wei, X., Zhang, X., & Li, C. (2017). Single continuous near-infrared laser-triggered photodynamic and photothermal ablation of antibiotic-resistant bacteria using effective targeted copper sulfide nanoclusters. *ACS Applied Materials & Interfaces, 9*(36), 30470–30479.
116. Sun, Q., He, F., Bi, H., Wang, Z., Sun, C., Li, C., Xu, J., Yang, D., Wang, X., & Gai, S. (2019). An intelligent nanoplatform for simultaneously controlled chemo-, photothermal, and photodynamic therapies mediated by a single NIR light. *Chemical Engineering Journal, 362*, 679–691.
117. Younis, M. R., Wang, C., An, R., Wang, S., Younis, M. A., Li, Z.-Q., Wang, Y., Ihsan, A., Ye, D., & Xia, X.-H. (2019). Low power single laser activated synergistic cancer phototherapy using photosensitizer functionalized dual plasmonic photothermal nanoagents. *ACS Nano, 13*(2), 2544–2557.
118. Mohammed Sulaiman, A.-Z., Raoof Rahed, K., & Abdulahmeed Midhat, T. (2022). Detection of Human Herpesvirus 8 Antibodies in Women with Breast Cancer in Kirkuk city. Al-Kitab Journal for Pure Sciences, 3(2), 1–9. https://doi.org/10.32441/kjps.03.02.p1
119. Wang, X.-Q., Peng, M., Li, C.-X., Zhang, Y., Zhang, M., Tang, Y., Liu, M.-D., Xie, B.-R., & Zhang, X.-Z. (2018). Real-time imaging of free radicals for mitochondria-targeting hypoxic tumor therapy. *Nano Letters, 18*(11), 6804–6811.
120. Xu, Y., Qi, J., Yang, X., Wu, E., & Qian, S. Y. (2014). Free radical derivatives formed from cyclooxygenase-catalyzed dihomo-γ-linolenic acid peroxidation can attenuate colon cancer cell growth and enhance 5-fluorouracil′ s cytotoxicity. *Redox Biology, 2*, 610–618.
121. Liu, Y., Bhattarai, P., Dai, Z., & Chen, X. (2019). Photothermal therapy and photoacoustic imaging via nanotheranostics in fighting cancer. *Chemical Society Reviews, 48*(7), 2053–2108.
122. Li, Z., Liu, J., Hu, Y., Howard, K. A., Li, Z., Fan, X., Chang, M., Sun, Y., Besenbacher, F., & Chen, C. (2016). Multimodal imaging-guided antitumor photothermal therapy and drug delivery using bismuth selenide spherical sponge. *ACS Nano, 10*(10), 9646–9658.
123. Qin, F., Zhao, H., Li, G., Yang, H., Li, J., Wang, R., Liu, Y., Hu, J., Sun, H., & Chen, R. (2014). Size-tunable fabrication of multifunctional Bi 2 O 3 porous nanospheres for photocatalysis, bacteria inactivation and template-synthesis. *Nanoscale, 6*(10), 5402–5409.
124. Henderson, T. A., & Morries, L. D. (2015). Near-infrared photonic energy penetration: can infrared phototherapy effectively reach the human brain? *Neuropsychiatric Disease and Treatment*. https://doi.org/10.2147/NDT.S78182
125. Nam, J., Son, S., Ochyl, L. J., Kuai, R., Schwendeman, A., & Moon, J. J. (2018). Chemo-photothermal therapy combination elicits anti-tumor immunity against advanced metastatic cancer. *Nature Communications, 9*(1), 1074.
126. Maruoka, Y., Nagaya, T., Sato, K., Ogata, F., Okuyama, S., Choyke, P. L., & Kobayashi, H. (2018). Near infrared photoimmunotherapy with combined exposure of external and interstitial light sources. *Molecular Pharmaceutics, 15*(9), 3634–3641.
127. Antaris, A. L., Robinson, J. T., Yaghi, O. K., Hong, G., Diao, S., Luong, R., & Dai, H. (2013). Ultra-low doses of chirality sorted (6, 5) carbon nanotubes for simultaneous tumor imaging and photothermal therapy. *ACS Nano, 7*(4), 3644–3652.
128. Chen, F., & Cai, W. (2015). Nanomedicine for targeted photothermal cancer therapy: Where are we now? *Nanomedicine, 10*(1), 1–3.
129. Zhu, H., Li, J., Qi, X., Chen, P., & Pu, K. (2018). Oxygenic hybrid semiconducting nanoparticles for enhanced photodynamic therapy. *Nano Letters, 18*(1), 586–594.
130. Lu, K., He, C., Guo, N., Chan, C., Ni, K., Weichselbaum, R. R., & Lin, W. (2016). Chlorin-based nanoscale metal–organic framework systemically rejects colorectal cancers via synergistic photodynamic therapy and checkpoint blockade immunotherapy. *Journal of the American Chemical Society, 138*(38), 12502–12510.
131. Li, J., Xie, C., Huang, J., Jiang, Y., Miao, Q., & Pu, K. (2018). Semiconducting polymer nanoenzymes with photothermic activity for enhanced cancer therapy. *Angewandte Chemie International Edition, 57*(15), 3995–3998.
132. Cano-Mejia, J., Burga, R. A., Sweeney, E. E., Fisher, J. P., Bollard, C. M., Sandler, A. D., Cruz, C. R. Y., & Fernandes, R. (2017). Prussian blue nanoparticle-based photothermal therapy combined with checkpoint inhibition for photothermal immunotherapy of neuroblastoma. *Nanomedicine: Nanotechnology, Biology and Medicine, 13*(2), 771–81.
133. A. Samad, A., & B. Kanbar, C. (2022). Prevalence of Bronchial Asthma among Patients attending Tertiary Allergy center / Kirkuk / Iraq. Al-Kitab Journal for Pure Sciences, 3(2), 120–130. https://doi.org/10.32441/kjps.03.02.p10
134. Duan, X., Chan, C., Guo, N., Han, W., Weichselbaum, R. R., & Lin, W. (2016). Photodynamic therapy mediated by nontoxic core–shell nanoparticles synergizes with immune checkpoint blockade to elicit antitumor immunity and antimetastatic effect on breast cancer. *Journal of the American Chemical Society, 138*(51), 16686–16695.