Recent advance in near-infrared/ultrasound-sensitive 2D-nanomaterials for cancer therapeutics

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ABSTRACT In recent years, the emerging two-dimensional (2D) nanomaterials have shown great potential for a variety of applications such as electronics, catalysis, supercapacitors, and energy materials. In the biomedical arena, these nanomaterials, especially 2D-ultrathin nanomaterials, have also been regarded as promising nano-carriers and/or diagnostic agents for cancer diagnosis and treatment, owing to their remarkable mechanical, photothermal, and optical properties. In this review, we provide the recent development of the nanoplateforms based on near-infrared/ultrasound-sensitive 2D-materials, representatively such as graphdiyne (GDY), black phosphorus, transition metal dichalcogenides (TMDs), and antimonene, for non-invasive cancer therapeutics including photothermal, photodynamic and sonodynamic approaches. The general properties of these 2D nanomaterials linking to biomedical interests are first introduced, followed by the fabrication processes of diverse nano-platforms and related outcomes of cancer diagnosis and treatments. We also outline the current challenges and prospects of the 2D materials for non-invasive approaches to cancer treatments in the future.

Keywords: nanomaterial, 2D layered materials, photothermal therapy, photodynamic therapy, sonodynamic therapy

INTRODUCTION

Currently, cancer is considered as a major cause of human death worldwide, and the development of new anticancer therapy has drawn more and more scientists' attention [1]. At this stage, several traditional methods applied in clinical treatment include tumor surgery,

chemotherapy, and radiotherapy. However, these therapy methods are highly invasive and always subject to several inherent limitations [2,3]. Tumor surgery suffers from the incomplete clearance of cancer cells and scar formation, while both chemotherapy and radiotherapy can cause severe damage to the normal tissues, resulting in insufferable pains. Also, these invasive approaches cannot effectively avail against the metastasis of cancer cells. Therefore, the discovery of new, effective and secure therapy methods is still imperative.

In recent years, non-invasive approaches such as photothermal therapy (PTT), photodynamic therapy (PDT), and sonodynamic therapy (SDT), have gained increasing attention and offer great potentials for cancer treatment [4,5]. This is mainly ascribed to several advantages of these therapies such as reducing side effects, eliminating unnecessary biopsies and improving therapy outcomes, as compared with the traditional treatment approaches, such as chemotherapy and tumor surgery. Typically, the operation of these non-invasive treatments requires the assistance of additional agents (e.g., photosensitizers for PDT and sonosensitizers for SDT) that can respond to external stimuli (e.g., light, heat, ultrasound, magnetic field and electrical field) [6–8]. Major mechanisms of these methods to kill cancer cells involve the elevation of local hyperthermia, generation of reactive oxygen species, controllable release of drugs/agents and enhancement of membrane permeability, etc. [9,10].

Nanotechnology, especially nanomedicine and various nanomaterials, has been rapidly developed for biomedical

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applications in the past decades [11–13]. At the current stage, a variety of nanoplateforms with different functions have been subsequently demonstrated, including two-dimensional (2D) layered nanomaterials, 3D nanoparticles (NPs), micelles, liposomes, dendrimers, and carbon nanotubes [14–16], potentially applied for drug delivery, gene therapy, stem cell therapy, bioimaging and biosensing, etc. Among those, 2D nanomaterials, represented by 2D-ultrathin layered nanomaterials, have been gained ever-increasing interests of the researchers in the past 15 years, in the light of the successful applications of graphene-related materials [17–20]. So far, diverse emerging 2D materials including graphdiyne (GDY), black phosphorus (BP), transition metal dichalcogenides (TMDs), antimonene (AM) and boron nitride (BN), have been reported and demonstrated for various applications in the recent years [21–24]. For example, BP has been regarded as a perfect alternative for graphene in many fields including photonics and optoelectronics [25–30], owing to its remarkable mechanical, photoelectric, and physicochemical properties. In addition, these 2D layered nanomaterials possess good biosafety including biocompatibility and biodegradability, making them suitable nanoplateforms for biomedical applications including cancer theranostic and biosensing. In the field of cancer treatment, these nanoplateforms typically act as carriers for antitumor drugs and theranostic agents, and more importantly, the pre-loaded antitumor drugs and agents can be released into tumor sites in a controllable manner thereby diminishing the adverse effects and toxicity [31,32]. Moreover, the inherent characteristic of nanoplateforms can remarkably improve the membrane permeability and cellular uptake, which can also benefit the suppression of cancer metastasis.

In light of the wide use of various nanomaterials in cancer diagnosis and therapy, many studies in this field have been extensively published [33–35]. In this work, we update the latest research advances in the 2D nanomaterials for non-invasive therapy from the perspective of biomedicine science, more precisely in the fields of PTT, PDT, SDT and multimodal therapy based on these approaches for cancer treatment. First, the fundamental properties of these emerging nanomaterials related to their application in non-invasive approaches are briefly introduced; then, the state-of-the-art development of these nanomaterials alliance with PTT, PDT, and/or SDT is individually discussed, with a detailed description of the fabrication processes and associated cancer therapy efficacy. We also outline the prospects of the 2D materials in cancer treatment and the main challenges that need to

be overcome.

EMERGING 2D MATERIALS AND THEIR PROPERTIES FOR NON-INVASIVE APPROACHES

The past decade has witnessed the emergence of 2D materials, and many of them exhibit excellent mechanical, electronic, and optical properties [36–38]. Generally, the properties of 2D nanomaterials are diverse, dimension- and composition-dependent, enabling the promise for versatile applications [39–41]. In spite of this, for a specific application, e.g., non-invasive cancer therapy, there are also commonalities among different nanomaterials. For example, good biocompatibility and biodegradability are common concerns for nanomaterials used in the biomedical field [42,43]. Besides, the properties of nanomaterials are supposed to be readily tailored and modulated, which would allow further modification and functionalization for specific biological interests. More importantly, a good response of these 2D nanomaterials to external stimulus (e.g., heat, magnetic field, near-infrared (NIR) region laser irradiation, and ultrasound) is the prerequisite condition for their applicability in the non-invasive therapeutic processes [44–46]. As several studies have reported the distinctive characteristics of the aforementioned 2D materials [33–35], in this section we briefly provide an overview of different classes of these materials (Fig. 1), their structural features and properties linking to their biological endpoints.

Graphene-based nanomaterials

To date, the graphene family is still the most heavily studied 2D layered materials for biomedical and optical applications [50–54], generally including graphene, graphene oxide (GO), reduced GO (rGO). The single layer of pristine graphene has a hexagonal lattice plane structure with sp^2 hybrid orbitals. The strong in-plane C–C bond and the out-of-plane π bond among the graphene matrix result in a delocalized network of electrons. Because of these unique electronic properties, graphene is widely studied as an ideal 2D semiconductor with zero bandgap. It also exhibits light absorption from the ultraviolet through the NIR, which is proportional to the number of layers [55,56]. In comparison with carbon nanotube-based materials, the graphene family possesses a higher surface area, endowing them with further functionalization [57,58]. The pristine graphene has been extensively applied for various biomedical applications including gene delivery [59,60], tissue engineering [61] and biosensing [62]. For example, Zeng *et al.* [62] reported a

Figure 1 Structural representation of 2D layered materials. (a) Graphene, (b) GDY, (c) black phosphorus, (d) TMDs, (e) two stable allotropes of antimonene, (f) hexagonal boron nitride. (a, c, d, f) Reprinted with permission from Ref. [47], Copyright 2019, the Royal Society of Chemistry; (b) Reprinted with permission from Ref. [48], Copyright 2018, American Chemical Society; (e) Reprinted with permission from Ref. [49], Copyright 2016, the Royal Society of Chemistry.

biosensor combining graphene and gold for detecting unlabeled ssDNA mainly *via* the π - π stacking interaction between graphene layers and ssDNA molecules.

As compared with pristine graphene, GO has higher wettability and higher affinity and thus shows greater potential as a drug carrier, due to the presence of higher content of oxygen functional moieties (e.g., $-\text{COOH}$ and $-\text{OH}$). These reactive moieties can be further functionalized to improve the hydrophilicity and solubility, making GO more suitable for drug loading [63]. Polyethylene glycol (PEG) functionalized GO nanocomposite (NGO-PEG) has been reported to have greater solubility and enhance the anticancer effect as a carrier of chemotherapeutic drugs [64]. Also, motivated by its strong NIR-absorbing ability, GO nanosheets are widely reported to be used as PTT agents [65]. Other feasible applications of GO in biomedical domains include tissue engineering and immunosensing [66,67]. rGO possesses more sp^2 carbon than GO, thereby exhibiting a higher NIR absorbance that can be opportunely exploited for non-invasive therapy [68,69]. Despite the less content of oxygen functional groups than GO, rGO can still interact with external drugs or agents *via* van der Waals forces, hydrophobic or π - π stacking interactions. Many studies have shown that antitumor drugs, e.g., doxorubicin (DOX), can be effectively adsorbed onto the rGO surface *via* hydrophobic and π - π stacking interactions [70]. The tests of rGO on tissue engineering and bio-sensing have been also heavily reported, owing to the availability and

excellent electrical conductivity [71]. For example, rGO-based biosensors show promising application in rapid and accurate detection of hormones [72]. Collectively, the graphene family abovementioned have been successfully utilized in a large number of applications including drug delivery, biosensing, bioimaging, and antibacterial activity [68,73,74].

Graphdiyne

GDY is another rising star of 2D carbon-based nanomaterial and firstly synthesized by Li *et al.* [75] *via* a coupling reaction among hexaethynyl benzene in 2010. The essence of GDY is not a graphene-based but graphene-like material. Unlike graphene-based materials, GDY possesses two classes of carbon atoms, sp - and sp^2 -hybridization from its acetynyl moiety and benzene ring, respectively. The fundamental structural unit of GDY is a triangle, three sides of which are made up of two acetynyl groups connecting neighboring benzene. This new carbon-based allotrope has been found to exhibit many fascinating mechanical and photoelectric properties including broad optical absorption and high photothermal conversion (PTC) efficiency [76,77]. Various GDY-based nanomaterials with different dimensions and morphologies (e.g., nanofilms [78], nanowires [79], nanotube [80], nanowalls [81], ordered stripe arrays [82], and 3D framework [83]) have been also reported. To modify the bandgap of GDY as well as its properties, a large number of approaches have been successfully developed so far,

including doping of boron/nitrogen [84,85], nanoribbon architectures [86], adsorption of guest molecules [87,88] and chemical reaction (e.g., hydrogenation [89], fluorination [90] and metal decoration [91]). Capitalizing on their excellent properties, GDY and its derivatives have been widely studied on optics, energy storage, separation/purification, detectors and catalysis [48,92]. Their biomedical applications have rapidly been expanded to various fields including radiation protection, antitumor, tissue engineering, biosensing, and bioimaging [93–95].

Xenes

Several 2D-monoelemental materials, commonly categorized as Xenes such as phosphorene, arsenene, antimonene, germanene, stanene, and bismuthene, have been developed and attracted dramatically increasing attention in recent years. Phosphorene, also called as BP, is comprised of a single phosphorus element with a stable allotrope. Different from graphene with a zero bandgap, BP possesses a remarkably broad bandgap that is proportional to its layer number (from 0.3 eV in bulk form to 2.0 eV in the monolayer) [96,97], and thus can absorb energy ranging from ultraviolet to infrared light regions. Benefitting from this remarkable NIR extinction and unique photoelectronic property, BP exhibits high PTC efficiency that distinguishes it from other 2D nanomaterials such as graphene-related derivatives. Currently, BP has been considered as an excellent supplement for graphene-related materials and widely exploited in the optoelectronic fields such as laser mode-locking [27,98–100], field-effect transistors [101–103], and non-linear optics [104,105]. The large channel size of 0.308 nm can allow BP for further decoration of metal ions with appropriate sizes, e.g., sodium, lithium, and aluminum, endowing them with impressive advantages in the fields of energy storage and conversion [106–110]. Unlike other 2D nanomaterials possessing planar nanostructure, e.g., graphene, BP nanosheets have a puckered honeycomb structure thereby having a larger surface-area-to-volume ratio. This special structure makes BP-based nanoplateforms promising candidates for nanocarriers [111]. Moreover, it is well-known that the phosphorus is a vital element in organisms involving many important functions (e.g., energy transformation and the construction of nucleic acids), and thus BP nanomaterials have been proposed to have better biocompatibility and biodegradability than graphene-related materials [112–115]. Preliminary studies have demonstrated that BP can substantially decompose to nontoxic intermediates such as phosphates or phosphites. These fancy properties in-

cluding controllable bandgap, high carrier mobility, large surface-area-to-volume ratio, and good biodegradability as well as biocompatibility, render BP an ideal candidate for biomedical application [116–120].

AM is another class of recently developed 2D Xenes based on monoelemental pnictogen element, and its nanolayers have been found to possess excellent properties including high thermal conductivity, controllable bandgap, high loading capacity and remarkable PTC efficacy [121–123]. Nano-scaled AM can be prepared *via* mechanical or liquid-phase exfoliation (LPE) of antimony crystals [124]. Zamora's group [125] demonstrated the use of LPE with the assistance of sonication to prepare a few-layer AM with high stability and large lateral dimensions. Owing to its extremely strong light-absorbing property [126–128] and high PTC efficiency, the nanomaterials based on AM, e.g., quantum dots (QDs) and nanosheets, have shown great promise for novel PTT agent. It is found that the PTC efficiency of antimonene is much higher than that of many other 2D nanomaterials such as GO, Au nanorods, and BPQDs [120,129]. Preliminary studies have demonstrated that AM has relatively low toxicity, portending its huge potentials in the biomedical and bioimaging fields [129]. Nevertheless, AM can rapidly degrade in the physiological microenvironment, limiting its direct applicability in healthcare. To address this, several different strategies have been demonstrated to improve its poor stability, such as modification with PEG, conjugation with biomolecules, or the cooperation of cell membrane camouflage [120,130].

Transition metal dichalcogenides

TMDs broadly refer to 2D-nanomaterials that have one layer of transition metals (Group 4–10, e.g., Ti, Hf, Nb and Mo) sandwiched between two layers of chalcogen (S, Se and Te) to form a hexagonal lattice, with a typical formula of MX_2 . To date, several approaches to synthesize TMDs have been reported, which are generally categorized into two classes: top-down and bottom-up methods. Typical top-down methods mainly include mechanical exfoliation [131,132], chemical exfoliation [133] and LPE. All these approaches have their respective pros and cons, e.g., mechanical methods are always subjected to inefficiency and time-consuming issues [134,135], while chemical exfoliation is one of the simple and convenient approaches to make single or few-layer TMDs but involve the difficulty in the clearance of residual chemicals, e.g., Li [136]. Solvent exfoliation under ultrasonication can prepare TMD nanosheets in a large scale [137], and more

encouragingly, these as-prepared nanosheets tend to distribute individually rather than re-aggregate together [138]. The bottom-up methods include solvothermal and hydrothermal approaches [139]; the former can be used for large-scale synthesis but the ligands used in the process are hard to remove, while the latter is more efficient due to the ease of fabrication and wide applicability [140,141]. Chemical vapor deposition is one of the most attractive bottom-up methods for preparing 2D layered TMDs with less defects, and also shows good controllability of monolayer synthesis [134,142].

Depending on the compositions and their specific characteristics, TMDs have been demonstrated as high-potential materials in a variety of areas such as chemistry, materials science and photoelectronics [143–145]. In addition, ultrathin monolayer and multiple layers of TMDs have intrinsic high-absorbance in the NIR region and possess large surfaces with low toxicity. These merits offer TMDs many opportunities for biomedical applications [146–148]. For instance, Urbanova and Pumera [149] recently summarized the potential use of TMDs in the field of biomedical and bioimaging, and Zhang *et al.* [150] reported the functional TMDs nanomaterials for chemo-photothermal therapy.

MXene

MXenes, a novel family of 2D solid crystals was firstly introduced by Gogotsi and co-workers in 2011 [151]. A typical MXene is constituted by transition metal carbides, nitrides, and carbonitrides, with a structural formula of $M_{n+1}X_n$ ($n=1,2,3$), in which M is an early transition metal (e.g., Ti, Zr, Hf, V, Ta, Cr, Mo) and X corresponds to carbon and/or nitrogen. Currently, more than 70 forms of MXenes have been reported for diverse applications, most of which are synthesized through wet chemical etching of the A group (12–16 periodic table elements) from the layered ternary carbides of MAX phases. This special synthesis method also results in abundant functional groups, e.g., hydroxyl (–OH), oxygen (–O), or fluorine (–F) depositing on MXenes. It has been found that these groups play important roles in defining MXenes' properties such as hydrophilicity and adsorption capability towards cations or positively charged molecules. MXenes can also be subjected to the modification with polymer-based materials (e.g., PEG [152], polyvinylpyrrolidone (PVP) [153] and soybean phospholipid (SP) [154]) or decoration with inorganic NPs (e.g., mesoporous-silica nanoparticles (MSNs) [155] and Fe_3O_4 [156]). The high surface-to-volume ratio enables MXene nanosheets to be potential drug carriers with abundant anchoring sites and

reservoirs. Owing to their ultrathin layered structure and broad absorption in the NIR region including the first (650–950 nm) and second biological window (1000–1350 nm), MXenes possess fascinating physico-chemical properties, e.g., photothermal conversion and localized surface plasmon resonance (LSPR) for biomedical applications such as PTT, PDT and cellular imaging [153,157].

Boron nitride

Apart from the above materials, several other types of emerging 2D materials have been studied for cancer therapy as well as other biomedical interests [24,51,158]. The ultrathin hexagonal BN (h-BN), especially its monolayer as known as “white graphene”, has recently aroused ever-increasing interests of researchers. h-BN contains two atoms of boron and nitride with a stoichiometry ratio of approximately 1:1, with a layered structure similar to graphene. Single or few-layered h-BN possesses a remarkably large bandgap (5–6 eV) due to the strong polarity of the B–N bond localizing the electronic states [159]. Initially, the solubility and chemical inertness of h-BN limit its wide applicability in biomedical domains. Nevertheless, various methods have been developed in the past decade to overcome these limitations, including surface modification with hydrophilic groups [160,161], immobilization with guest molecules [162,163], and solid chemical reaction to alter the hydrophobicity [123]. Compared with its carbon counterparts such as graphene, h-BN possesses relatively lower cytotoxicity [164,165]. These characteristics of h-BN, with the coexistence of excellent mechanical properties and high thermal conductivity, allow BN-based nanomaterials ideal platforms for cell proliferation, drug delivery, and tissue engineering [166,167].

2D NANOMATERIALS FOR NON-INVASIVE THERAPY

Photothermal therapy

PTT is currently the most studied and described non-invasive therapeutic approach. In principle, PPT kills cancer cells and damages tumor tissue *via* located hyperthermia generated by light-absorbing agents under NIR light irradiation [168,169]. PTT possesses significant merits of eliminating the toxicity and avoiding the side-effect to normal tissues surrounding the tumor sites, because hyperthermia is produced only when NIR light is applied and where the light-absorbing agent is present in body tissues. This therapeutic approach has been ex-

tensively combined with other treatment techniques, such as chemotherapy [170,171], gene therapy [172–174] and immunotherapy [175–177] to improve the treatment efficacy, because local hyperthermia can simultaneously improve the permeability of cell membrane and promote drug/gene releasing at the tumor sites. Besides, the NIR light-responsive drug released in the tumor site could reverse multidrug resistance mechanisms such as drug efflux.

The light-absorbing agents used in PTT widely contain many organic materials (e.g., indocyanine green (ICG), heptamethine cyanine and phthalocyanine) and inorganic materials (e.g., sulfide NPs and gold NPs) [178,179]. Similar to these light-sensitive agents, most of the 2D nanomaterials also possess excellent light absorption properties and thus can exhibit great thermal conductivity under the NIR light irradiation [180–182]. Also, these nanomaterials can synchronously act as nano-carriers or nanocapsules for the delivery of drug/gene or other agents, thereby devoting to cancer cell apoptosis and necrosis. The recent progress of various 2D materials in PTT was summarized in Table 1.

Graphene-based nanomaterials

Graphene nanomaterials have been extensively demonstrated for many photothermal uses, due to the high absorbance in the NIR region [183,184]. For instance, Chen *et al.* [185] summarized the utilization of graphene for PTT prior to the year 2016. The photothermal effect of graphene under NIR light has been shown to enhance tumor chemotherapy by improving the sensitivity of tumor cells to DNA-damaging drugs (such as DOX) and promoting the targeted release of drugs [186,187]. Compared with PTT effect alone, the applications of graphene-based platforms as therapeutic agents for both anti-tumor drug delivery and PTT have been widely carried out [188,189]. Under one single treatment, these nano-matrixes exhibited multimodal therapeutic effects including PTT and chemotherapy, leading to a strong antitumor efficacy. It was also found that graphene-mediated synergistic PTT and immunotherapy showed enhanced effects in cancer treatment. Yan *et al.* [69] designed multifunctional PEGylated rGO-based nanosheets incorporating indoleamine-2,3-dioxygenase (IDO) for *in-situ* immune response in tumor sites and folic acid (FA) for tumor targeting. In this case, PEG-rGO-FA-IDO nanosheets effectively triggered the PTT effect under NIR laser irradiation, and simultaneously induced the immunological response with high tumor-specific targeting, resulting in enhanced therapeutic efficacy.

The zero-energy bandgap of graphene normally prevents its wide applicability in the biomedical fields. However, when it comes to the size of QDs, graphene materials are endowed with enhanced physicochemical properties such as discrete bandgap and great photoluminescence, while also maintaining its pristine advantages, e.g., good biocompatibility and high chemical stability [15,190]. Yao *et al.* [191] demonstrated the potential use of GQDs for PTT combining magnetic-mediated hyperthermia therapy. GQDs were used to coat the magnetic MSN (MMSN) to construct an MMSN/GQDs multifunctional platform for drug delivery, PTT and magnetic-mediated hyperthermia. This design enabled remarkable temperature elevation for tumor hyperthermia therapy, due to the dual hyperthermia effects from MMSN and GQDs. Apart from inorganic materials, e.g., MMSN, various organic polymers such as PEG and PEI are always selected to modify QDs to fabricate a suitable delivery system. Nevertheless, many polymers have issues of long-term toxicity and non-degradability. To address this, Yang *et al.* [192] reported the use of biodegradable charged polyester vectors (BCPVs)-functionalized GQDs for co-delivery of DOX and siRNA to treat pancreatic cancer (Fig. 2). MiaPaCa-2 cells treated with this fluorescein-labeled GQDs-based nanocomplex displayed strong fluorescence intensities of DOX, indicating the promising co-delivery of drugs and genes.

Apart from the high absorbance, GQDs could be developed for photoacoustic imaging (PAI) or combined with other imaging contrast agents to achieve multimodal imaging-guided cancer therapy [193,194]. In Xuan's work [195], a versatile nano-probe based on GQDs and Au nanodots was formed for PAI and computed tomography (CT) imaging. This nanoprobe displayed great PTC efficiency as high as 51.3% with relatively low cytotoxicity observed.

GDY

Recent research findings have shown that GDY-based nanomaterials can also play multimodal roles including drug carrier, PTT agent and contrast agent for cancer treatment [196,197]. In a typical work, Li *et al.* [94] reported the use of GDY as a PTT and contrast agent for both PTT and PAI. Interestingly, it is noted that the GDY-PEG nanomaterials showed a better mass extinction coefficient (ca. $10.1 \text{ L g}^{-1} \text{ cm}^{-1}$) under 808 nm laser irradiation than GO materials [198], and also exhibited a higher PTC efficiency (ca. 42%) than other traditionally organic PTT agents [199–201]. This could be related to multiple conjugated electronic structures of GDY, which

Table 1 Summary of 2D nanomaterials for PTT applications

Therapeutic platform	2D nanomaterials	<i>In vitro</i>	<i>In vivo</i>	PTC efficiency (%)	Therapy strategy	Ref.
rGO/(PLL/PASP)n@DOX	rGO nanosheets	Hela cell line	–	24.30	PTT, chemotherapy	[188]
GO(PEG-PpIX)	GO nanosheets	4T1 cell/Hela cell line	4T1 tumor-bearing mice	–	PTT, PDT, chemotherapy	[189]
PEG-rGO-FA-IDOi	rGO nanosheets	CT26 cell line	CT26 tumor-bearing mice	–	PTT/immunotherapy	[69]
DOX-MMSN/GQDs	GQDs	4T1 cell line	–	–	PTT/chemotherapy/magnetic hyperthermia therapy	[191]
GQD/DOX/BCPV/siRNA	GQDs	MiaPaCa-2 cell line	–	–	PTT/chemotherapy/gene therapy	[192]
Au/DOX@GQDs-FA	GQDs	Hela/A549 cell line	Hela tumor-bearing mice	51.31	PA/CT imaging-guided PTT/chemotherapy	[195]
GDY-PEG	GDY nanosheets	4T1 cell line	4T1 tumor-bearing mice	42.00	PA imaging-guided PTT	[94]
GDY/DOX	GDY nanosheets	MDA-MB-231/MCF-7/A549 cell line	MDA-MB-231 tumor-bearing mice	42.00	PTT, chemotherapy	[95]
BP-DEX/PEL-FA/Cy7	BP nanosheets	4T1 cell line	4T1 tumor-bearing mice	41.00	NIRE/PA imaging-guided PTT	[219]
BP@PEG/Ce6	BP nanosheets	Hela cell line	Hela tumor-bearing mice	43.60	PTT/PDT	[220]
BP/DTX@PLGA	BPQDs	4T1-LG12 cell line	4T1-LG12 lung metastatic tumors	–	PTT/chemotherapy	[231]
BPQDs-PEG-FA/DOX	BPQDs	Hela cell line	Hela tumor-bearing mice	–	PTT/chemotherapy	[232]
MoS ₂ -SS-HA-CPT	MoS ₂ nanosheets	A549 cell line	A549 lung cancer cell-bearing mice	28.80	PTT/chemotherapy	[244]
PEGylated-MoS ₂ /Cu _{1.8} S	MoS ₂ nanosheets	A549 cell line	A549 lung cancer cell-bearing mice	32.50	PTT/chemotherapy	[245]
NIR-CD/MoS ₂	MoS ₂ nanosheets	Hela cell line	4T1 tumor-bearing mice	78.20	PTT/chemotherapy	[246]
MoS ₂ @PANI	MoS ₂ QDs	4T1 cell line	4T1 tumor-bearing mice	31.60	PTT/RT ^a	[248]
DOX-POV-MoS ₂ -Tf	MoS ₂ nanodots	HepG2 cell line	–	–	PTT/chemotherapy	[249]
WS ₂ -Ga ³⁺ -PEG	WS ₂ nanosheets	HepG2 cell line	HepG2 tumor-bearing mice	–	PTT	[250]
WS ₂ -IO/S@MO-PEG	WS ₂ nanoflakes	4T1 cell line	4T1 tumor-bearing mice	–	PTT/RT	[251]
DOX@Fe(III)@WS ₂ -PVP	WS ₂ nanosheets	HT29 cell line	HT29 tumor-bearing mice	39.10	PTT/chemotherapy	[252]
Ti ₃ C ₂ -SP	Ti ₃ C ₂ nanosheets	4T1 cell line	4T1 tumor-bearing mice	–	PTT/chemotherapy	[154]
DOX/Ti ₃ C ₂ @mMSNs-RGD	Ti ₃ C ₂ nanosheets	HCC cell line	HCC-tumor-bearing mice	23.20	PTT/chemotherapy	[155]
Ta ₄ C ₃ -SP	Ta ₄ C ₃ nanosheets	4T1 cell line	4T1 tumor-bearing mice	44.70	PTT	[266]
Ti ₃ C-PEG	Ti ₃ C nanosheets	A375/MCF-7 cell line	–	87.10	PTT	[152]
MXene QDs	MXene QDs	Hela cell line	Hela tumor-bearing mice	52.20	PTT	[267]
PEG-coated AMQDs	AMQDs	MCF-7/Hela cell line	MCF-7 tumor-bearing mice	45.50	PTT	[120]
AM-PEG/DOX NSs	AM nanosheets	MCF-7 cells	MCF-7 tumor-bearing mice	41.80	PTT/chemotherapy	[129]
hBN/d-HA-Dox	hBN nanosheets	MDAMB-231 cell line	–	–	PTT/chemotherapy	[270]
Pd@OH-BNS	BN nanosheets	MCF-7 cell line	S180 tumor-bearing mice	–	PTT/chemotherapy	[271]
ICG-DOX/Gd-LDH	LDH	Hela cell line	Hela tumor-bearing mice	–	PTT/PDT	[274]
5-FU/Cu-LDH	LDH	HCT-116 colon cancer cells	HCT-116 colon tumor-bearing nude mice	53.1	PTT/chemotherapy	[275]

a) RT: radiation therapy.

Figure 2 Illustrations of preparing GQDs/DOX/BCPV/siRNA nanoplateforms for pancreatic cancer synergistic therapy. Reprinted with permission from Ref. [192], Copyright 2018, American Chemical Society.

offer enhanced photothermal efficiency. Moreover, as GDY is a typical electron-rich system, i.e., containing lots of conjugated phenyl and alkynyl moieties, external biomolecules or agents such as antitumor drug DOX can be firmly loaded onto the GDY surface *via* π - π stacking and electrostatic interactions. Recently, Zhao's group [95] reported a GDY-based drug delivery system for both chemotherapy and PTT (Fig. 3). Remarkably, it was noted that the loading content of anticancer drug in GDY nanomaterial was higher (ca. 38%) than that of pristine graphene reported in other studies. The drug-releasing kinetic studies showed that DOX was efficiently released from the prepared DOX-GDY nanocomposite at acidic conditions and under NIR irradiation. Some studies also depicted that GDY possesses a stronger free radical scavenging ability under X-ray irradiation than GO, which is mainly attributed to its unique sp-hybridized acetylenyl moieties [202,203]. This radiation protection ability could imply promising potentials of GDY nanomaterials combining with radiotherapy in cancer treatment, which is worth further investigation.

Xenes

In the past five years, many efforts have been made to synthesize and modify BP for various applications [204–207], particularly in the field of photoelectronics [207–211] and biomedicine [212,213]. Moreover, BP na-

nosheets exhibit greater PTC efficiency than graphene-related materials and thus receive considerable attention for biomedical applications [214,215]. Similar to graphene, the photothermal property of BP can be further applied to promote drug release behavior for enhancing the therapeutic effect. For instance, this promotion behavior has been exploited to fabricate light-responsive hydrogel-functionalized BP nanocomposites for a controlled anti-tumor drug release [7,216]. With a honeycomb-like structure and large surface, BP can easily allow further modification and functionalization for intended multimodal-therapy applications [217,218]. BP nanomaterials are subjected to the issue of its stability and rapid degradation, but the modification of BP with other agents and polymers always helps to address this issue. For example, Deng and co-workers [219] synthesized functional BP nanosheets with dextran (DEX) and branched poly(ethyleneimine) (PEI) for PA/near-infrared fluorescence (NIRF) imaging and PTT. DEX and PEI were noted to improve the safety and biocompatibility of BP nanosheets, meanwhile endowing good solubility. Another research by Yang *et al.* [220] successfully fabricated PEG-functionalized BP that can exert a dual anti-tumor effect of PTT/PDT. In their work, a high PTC efficiency of 43.6% was achieved, similar to that of other BP-related reports. The pre-loaded PEG also endowed this BP-based nanocomposite good biocompatibility and physiological

Figure 3 Illustration of GDY/DOX combining PTT and chemotherapy treatment. Reprinted with permission from Ref. [95], Copyright 2018, American Chemical Society.

stability, thereby improving the therapy efficacy. Recent studies revealed that polydopamine (PDA), a universal coating material [221,222], can be used to encapsulate BP and enhance the stability of BP nanosheets, resulting in the improvement of the PTT effect. Our previous study has shown that PDA modification could greatly improve the PTC efficiency of BPQDs from 22.6% to 64.2% (~2.84 fold higher) [223]. It is known that the PDA surface has an abundant functional group that can be used for further functionalization [224,225]. Capitalizing on this feature, the PDA-modified BP can be readily decorated with specific ligands, e.g., aptamers for tumor targeting purpose [226].

BPQDs utilized as photothermal agents have also been reported in recent years [199,227]. Because of their superior physicochemical properties, they have shown the possibility for combined therapy, e.g., chemotherapy, immunotherapy, PTT and PDT [228–230]. One recent study depicted the use of poly(lactic-co-glycolic acid) (PLGA)-functionalized BPQDs as photothermal agents and drug carriers [231]. Similarly, Luo *et al.* [232] demonstrated FA-functionalized BPQDs for tumor-targeted synergistic chemotherapy/PTT. In their results, those multimodal BPQDs-based nanoagents displayed good biocompatibility and showed strong potential for drug delivery and chemotherapy/PTT. Functional molecules can also adsorb onto the surface of BPQDs *via* non-covalent interactions to achieve multi-function applications, i.e., different kinds of imaging contrast agents can be combined with BPQDs to realize multimodal imaging-guided PTT. Zheng *et al.* [233] reported a theranostic agent for PAI/magnetic resonance imaging (MRI)-guided

cancer PTT and PDT based on poly(allylamine) (PAH)-modified BPQDs, immobilizing Prussian blue (PB) for great T1-weighted MRI. These unique NIR absorption properties of the as-designed nanoagents not only permitted PAI but also ensured great tumor inhibition activity.

Similarly, another type of Xene AMQDs has shown huge potentials as biosensors for cancer diagnosis [234] and photothermal agents for PTT, due to its extremely strong NIR absorption [126,235]. Interestingly, the PEGylated AMQDs were found to exhibit higher PTC efficacy (45.5%) than many 2D-nanomaterials including graphene (25%), MoS₂ (27.6%), and BPQDs (28.4%) [120]. Moreover, AM has also been shown to have superior PA properties than many other nanomaterials, e.g., BP, rGO and TMDs, rendering it a unique PAI contrast agent to achieve multimodal theranostics platform [236]. For instance, PEG-functionalized AM nanosheets have been demonstrated to be a superior drug carrier for PAI-guided tumor synergistic therapy [129]. Benefitting from the high PTC efficiency (41.8%) and high drug loading capacity (150.0%), the as-prepared AM-based NPs displayed excellent antitumor efficacy when used to treat MCF-7-tumor-bearing mice model (Fig. 4).

Transition metal dichalcogenides

2D TMD nanomaterials have been successfully applied for a variety of biomedical applications such as biosensing, bioimaging and cancer treatment [237–239], owing to their high specific surface areas, great NIR absorbance and low toxicity [240,241]. MoS₂, as one prototypical TMD nanomaterial, has been widely utilized as photo-

Figure 4 *In vivo* ultrasound/PA (a) and fluorescence (b) images of MCF-7 breast tumor-bearing mice after injection of AM-PEG NSs and Cy5.5-labeled AM-PEG NSs, respectively. Reprinted with permission from Ref. [129], Copyright 2018, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

thermal agents [242,243]. In addition, the integration of MoS₂-based nano-platform with other treatment techniques (e.g., PTT and chemotherapy) can drastically enhance the efficacy of cancer therapy. Recently, Liu *et al.* [244] developed a MoS₂-based tumor-targeting nano-platform for synergistic chemotherapy/PTT (Fig. 5). Single-layer MoS₂ nanosheets were conjugated with hyaluronic acid (HA) *via* disulfide bridging to enhance its physiological stability. An antitumor drug, camptothecin (CPT), was then loaded onto the MoS₂-SS-HA nanosheets to fabricate a tumor-targeting drug delivery system. Such a nano-composite exhibited strong absorbance under

NIR irradiation, thereby showing a PTC efficiency up to 28.8%, which contributed to its potential for PTT cancer treatment. Other functional nano-composites can be integrated with MoS₂ for enhanced PTT efficacy. Meng *et al.* [245] found that the decoration of PEGylated MoS₂/Cu_{1.8}S can significantly improve the PTC efficiency, presumably due to the synergistic interaction between MoS₂ and Cu_{1.8}S. After loaded with DOX, the as-designed nanohybrids displayed excellent targeted chemo-photo-thermal therapy in tumor-bearing mice implanted with A549 cells. In another study, Geng *et al.* [246] reported a heterojunction of MoS₂ nanosheets and carbon dots

Figure 5 Illustration of preparing MoS₂-SS-HA-CPT nanocomposites for synergistic chemo-photo-thermal cancer therapy. Reprinted with permission from Ref. [244], Copyright 2019, BioMed Central Ltd. unless otherwise stated. Part of Springer Nature.

(CDs) to achieve an enhanced PTT performance. The produced CD/MoS₂ composite displayed much higher PTC efficiency (up to 78.2%) than that of single MoS₂ (38.3%).

Compared with 2D nanosheet form, MoS₂ QDs and nanodots have been found to possess admirable biocompatibility, ensuring their great potentials for biomedical applications [247]. This could be ascribed to the fact that the small size of MoS₂ QDs helps to improve the clearance in the body. Wang *et al.* [248] constructed a versatile nanoplatform based on MoS₂ QDs combining with organic polyaniline (PANI), which showed good compatibility in physiological environments. Similarly, Zhang's group [249] developed a nanohybrid based on the copolymer P(OEGA-co-VBA) (POV) and transferrin (Tf)-modified MoS₂ nanodots (POV-MoS₂-Tf) for a self-guided photothermal nanocarrier.

WS₂ is another widely studied TMD for noninvasive therapy due to its promising photothermal as well as electrical effects. As mentioned, those effects are mainly ascribed to the ambipolarity and direct bandgap in a single-layer form. Capitalizing on these, Song's work [250] demonstrated the use of WS₂ as photothermal agents combining with a hepatocellular carcinoma (HCC)-specific tumor marker GPC3, which could be applied for HCC tumor-targeting PTT with MRI/PAI. WS₂-based nanomaterials also have the advantage of added synergetic radiotherapy, as the high-Z elements of WS₂ can facilitate the transfer of radiation energy into the tumor [251]. Recently, Wu *et al.* [252] employed a DOX-loaded Fe(III) species-WS₂-PVP nanocapsule for synergetic cancer treatment. Under 808 nm laser irradiation, the Fe(III)@WS₂-PVP nanocapsule displayed a high PTC of 39.1%. Benefitting from the high PTC capability, the nanocapsule has achieved great synergetic therapeutic efficiency *via* the combination effects of chemodynamic therapy, PTT and chemotherapy.

Other analogs such as Bi₂Se₃ [253,254], Bi₂S₃ [255] and Bi₂Te₃ [256] also have been demonstrated as good alternatives to traditional photothermal agents. The unique optoelectronic properties of Bi₂Se₃ have endowed the potential to convert laser energy to heat [257]. Since the first investigation of Bi₂Se₃ on cancer treatment by Li *et al.* [258], this 2D material, especially its decoration with other nanomaterials, e.g., MoSe₂ [248], FeSe₂ [259], and selenocysteine NPs [260] has been widely exploited for enhanced and/or multimodal therapeutics. Shao and co-workers [261] designed an interesting Bi₂Se₃-loaded poly (*L*-lactic acid) (PLLA) membrane, which can be used as local plaster for the treatment of skin cancer. Because of

the good biosafety of PLLA, this new-type membrane showed no significant harmful effects on the human body. It is expected that this approach could be suitable for many different wearable devices for cancer treatment.

MXene

Like TMDs nanomaterials, ultrathin MXene nanosheets have been utilized as the photothermal agents [262,263]. For example, Ti₃C₂ nanosheets have been found to possess high PTC efficacy and good biosafety [264]. Given that the large surface area of MXene provides rich anchoring sites for antitumor drugs and other agents, they can also be designed as integrated nanoplatforms for synergetic PTT and chemotherapy [265]. In a representative study, Han *et al.* [154] developed a pH-responsive nanoplatform based on Ti₃C₂ MXene for combined chemotherapy and PTT. Ti₃C₂ MXene nanosheets were first loaded with SP to improve the biostability and to provide a large surface area for drug loading, followed by the loading of DOX. The results showed that DOX can be efficiently released from this Ti₃C₂-based nanoplatform upon NIR irradiation as well as in the acidic microenvironment, thereby underlining its suitability for cancer treatment.

Many specific proteins or peptides expressed surrounding tumor sites can be effectively loaded onto MXene nanosheets for tumor-targeting. An active HCC targeting nanoplatforms based on a functionalized Ti₃C₂ was described by Li and co-workers [155]. In this investigation, MSNs were first deposited onto the surface of Ti₃C₂ to improve the interfacial properties. Then arginine-glycine-aspartic acid (RGD), a peptide overexpressed on the surface of HCC cells, was covalently connected to the PEGylated Ti₃C₂@mMSNs for tumor targeting (Fig. 6). The results showed that the RGD-loaded nanosheets remarkably improved the fluorescence intensities, as compared with Ti₃C₂@mMSNs-PEG, i.e., in the absence of tumor-targeting peptide. This study also indicates that the surface modification of nanosheets with specific peptides or proteins can efficiently enhance intracellularly tumor-targeting endocytosis and inhibit tumor growth.

Other types of 2D MXenes such as Ta₄C₃ and Ti₂C can also be used as photothermal agents. Li and co-workers [266] synthesized theranostic Ta₄C₃-based nanostructures with dual PAI and CT imaging for PTT. The synthesized Ta₄C₃ nanosheets displayed a uniform size and higher PTC efficacy of 44.7% than Ti₃C₂ nanosheets. In another study, Szuplewska [152] reported that Ti₂C can be used as a highly efficient and selective PTT agent. After mod-

Figure 6 Schematic illustration of preparing $\text{Ti}_3\text{C}_2\text{@mMSNs-RGD}$ for synergistic chemo-PTT against HCC with potential PA-imaging guidance and monitoring. Reprinted with permission from Ref. [155], Copyright 2018, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

ification with PEG, the $\text{Ti}_3\text{C}_2\text{-PEG}$ achieved great biocompatibility under physiological conditions, and also exhibited highly efficient conversion in the NIR region. Besides 2D nanosheets of MXene, their QDs also offer tremendous potential for non-invasive therapy. For instance, the strong NIR absorption of Ti_3C_2 MXene QDs can lead to a remarkable PTC efficiency of 52.2%, and Yu *et al.* [267] employed Ti_3C_2 MXene QDs as a PTT agent. After treatment with Ti_3C_2 MXene QDs under the 808 nm laser irradiation, the tumor tissues of HeLa tumor-bearing mice were eliminated.

Other types of 2D nanomaterials

As mentioned early, h-BN nanosheets (h-BNNS) are structurally similar to graphene, and its surface can be readily modified and functionalized, normally *via* hydroxylation, to reduce cytotoxicity and improve their biocompatibility. For practical applications, this is crucial to make BN more suitable for biomedical applications [164,268,269]. Sharker and co-workers [270] designed a functionalized h-BN synergistic therapeutic nanoplat-form, in which h-BN loaded ICG was integrated with a tumor-targeting chemotherapeutic agent (d-HA-DOX) to achieve both PTT and chemotherapy. In another study, BNNS were developed as a drug delivery nanoplat-form combining Pd as a photothermal core to release DOX [271] (Fig. 7a–c). The investigation using the S180 tumor-bearing mice model showed higher antitumor efficacy of the Pd@OH-BNNS/DOX group with an inhibition rate of 87.2% compared with chemotherapy or PTT alone. However, the authors did not clarify the long-term toxicity in the use of Pd *in vivo*, as it is known that the intravenous injection of Pd could be more toxic than *via*

oral administration.

Layered double hydroxide (LDH), has been rapidly developing in recent years for biomedical applications, specifically in cancer theranostic. Researchers have found that high magnetic-moment metal ions (e.g., Gd^{3+} , Mn^{2+} and Fe^{3+}) could be easily doped into LDH monolayer for MRI. The as-designed Gd-LDH or FeMn-LDH can strongly promote MRI performance as compared with commercial MRI contrast agents for cancer diagnosis [272,273]. Meanwhile, LDH-based materials have been developed as a promising platform for imaging-guided PTT of cancer. In Guan's work [274], the PTT agent (ICG) and the antitumor drug (DOX) were incorporated with Gd-LDH to develop an NIR-sensitive nanoplat-form for MRI guided PTT and chemotherapy. Owing to the synergistic effects of Gd-LDH and ICG, a rapid temperature enhancement was achieved. In another work, Cu-doped LDHNPs (Cu-LDH) have been used for MRI-guided PTT, owing to their high PTC efficiency (up to 53.1%) [275]. These Cu-LDH nanosheets were further utilized as a drug carrier to load the anticancer drug 5-FU for synergetic PTT-chemotherapy.

Metal-organic frameworks (MOFs) are a new subclass of porous hybrid materials with higher crystallinity and regular pores, built from a metal connecting node (e.g., metal ions or clusters) and organic bridged ligands (e.g., carboxylate ligand or other negatively charged ligands). Both metal-cluster secondary building units (SBUs) and bridging linkers can be functionalized to enhance PTC efficiency [276]. As a typical MOF, PB exhibits high PTC efficiency, high photothermal stability, and good biocompatibility. Fu *et al.* [277] first demonstrated the PTT performance of $\text{PB}(\text{Fe}^{\text{III}}_4[\text{Fe}^{\text{II}}(\text{CN})_6]_3 \cdot n\text{H}_2\text{O})$ NPs upon

Figure 7 (a, c) Schematic illustrations of preparing Pd@OH-BNNS/DOX for combinational chemotherapy and PTT; (b) TEM images of OH-BNNS (1 and 2) and Pd@OH-BNNS (3 and 4). Reprinted with permission from Ref. [271], Copyright 2019, Elsevier B.V.

NIR light excitation. Wang *et al.* [278] fabricated a novel core-shell PB@MIL-100(Fe) dual MOFs (d-MOFs) NPs, which can serve as a T1-T2 dual-modal MRI contrast and fluorescence optical imaging (FOI) for PTT.

Photodynamic therapy

PDT is another photochemical-based local treatment, in which a light-sensitive agent, normally referring to a photosensitizer, is activated by light with appropriate wavelength and intensity. The activation of photosensitizer will allow for the photocytotoxic reaction with oxygen molecules to produce reactive oxygen species (ROS), which eventually result in local damage of proteins, fats and other molecules, thereby inducing apoptosis and/or necrosis [279–281]. Therefore, the presence of photosensitizers, oxygen, and light activation are three critical elements of PDT. In contrast to PTT, PDT is believed to be a more effective technique with good biocompatibility, high photochemical reactivity, and great photosensitive effect [282]. Moreover, PDT has a good selectivity of tumor therapy because photosensitizers generally accumulate in much higher concentrations in the pathological tissues than in normal tissues. Hence, the photocytotoxic reactions occur mainly surrounding tumor sites where the photosensitizers are distributed [283].

Up to now, many photosensitizers (e.g., porphyrin,

chlorine and phthalocyanine derivatives) have been widely reported for clinical or preclinical studies [284]. Nevertheless, the direct use of these photosensitizers is subject to several limitations, such as low yield of ROS generation and poor water solubility [285]. The spring-up of 2D materials can help to overcome these drawbacks, and some of them could be good alternatives to traditional photo-sensitizers. Firstly, nanomaterials, such as TiO₂ [286], Au nanomaterials [287,288], upconversion NPs (UCNPs) [289], possess superior biochemical characteristics, and their nanoplateforms can be utilized as agent carriers for loading and delivering various hydrophobic photosensitizer molecules [290]. Secondly, the nanomaterials with a specific size generally have the advantage of passive accumulation in tumor cells *via* the enhanced permeability and retention (EPR) effect. Therefore, the loaded photosensitizers would accompany these nanomaterials preferentially accumulating in the tumor sites to maximize the selectivity of therapy [291,292]. Moreover, several types of 2D nanomaterials such as QDs and 2D-nanosheets can be directly used as intrinsic photosensitizers due to their excellent PTC efficiency, enabling combined PTT effects. This will also accelerate blood flow and increase the supply of oxygen molecules in the microenvironment, thus improving the PDT efficacy [293,294].

Graphene

Since the first report by Dong *et al.* [295] demonstrating a PEGylated nano-GO (NGO) as the carrier of photosensitizer for PDT, graphene-related materials have been extensively studied for the loading and co-delivery of various photosensitizer molecules. Co-assembling with GO-based nanomaterials, photosensitizers can be released from the NGO upon NIR irradiation thus realized in a controlled manner at a desirable site [296]. Some summaries of the use of graphene in PDT have been given in other reports [297,298]. Herein, we provided the most recent work in this field. In Sun's work [299], PEGylated GO NPs (PEG-GO) were encapsulated with aggregation-induced emission (AIE) photosensitizers for cancer PDT. Their research showed greater ROS generation ability than that of PEG capsulated NPs in the absence of GO, indicating their great potential in the application of PDT. Recently, a therapeutic nanoplatform based on chitosan-modified rGO was designed for PTT/PDT/chemotherapy synergistic therapy [300]. IR820 dye, as a biocompatible phototherapeutic agent, and the antitumor drug DOX were co-loaded onto rGO nanoflakes to form a nanohy-

brid. CT26 carcinoma cell study on this nanohybrid has shown a controllable therapeutic performance by adjusting the ratio of IR820/DOX. The author claimed that the phototherapy was a superior contributor to cell apoptosis as compared with chemotherapy in the synergistic therapeutic system.

It is known that GQDs can generate reactive $^1\text{O}_2$ upon light irradiation, which makes them interesting candidates for PDT use [301]. In a typical work, Liu *et al.* [302] designed a PDT nanocomposite based on the conjugation of GOQDs with UCNPs; FA for tumor targeting and carboxybutyl triphenylphosphonium (TPP) for mitochondrion targeting were simultaneously attached to the UCNPs-GOQDs nanohybrids to ensure a dual tumor-targeting functionality. Due to the fairly small size, QDs can also be used for the decoration of large biomolecules, e.g., proteins or antigens, which can be applied to design novel pharmaceuticals for photo-immunotheranostics. For instance, PDA-stabilized GQDs-Ce6 was assembled on the surface of nanoimmunocores, revealing a high capability of photothermal and ROS generation effect. Hence, it can be used to trigger immune responses

Figure 8 Schematic illustrations of preparing PC@GCpD (Gd) nanohybrids for MRI/fluorescence bimodal imaging-guided photo-immunotherapy. Reprinted with permission from Ref. [303], Copyright 2019, Elsevier B.V.

by releasing endogenous tumor antigens to kill cancer cells [303] (Fig. 8).

Xenes

Similar to GQDs, the exfoliated BP nanocrystals are also capable of generating a large number of ROS under laser excitation and showed excellent antitumor effect [114]. Moreover, BPQDs and BP nanowires can be used as excellent photosensitizers due to their extensive light absorption through ultraviolet to NIR [304–306]. More importantly, BPQDs, especially those with diameters of less than 6 nm, show rapid renal clearance, ensuring their high efficiency and biosafety for biomedical applications [307]. To address the safety and degradation issue of BPQDs, PEG-functionalized BPQDs could be used for tumor-imaging and combined PTT/PDT treatment [228]. Therefore, PEGylated BPQDs significantly promoted the therapeutic efficacy in contrast to the use of PTT or PDT alone.

PDT traditionally has low efficacy in the treatment of hypoxic tumor cells, as the photosensitizers would fail to generate considerable $^1\text{O}_2$ due to the insufficient oxygen supply [308,309]. Liu *et al.* [310] reported a novel strategy to address this limitation *via* the incorporation of nanosheets with Fe-protoporphyrin IX (Heme). It is well-known that Heme can be served as an additional catalytic agent to convert H_2O_2 to O_2 *via* an *in-situ* decomposition process. Therefore, BP/Heme-based PDT agents can induce a cell apoptosis 8.7-fold more than that of BP nanosheets in the absence of Heme in a hypoxic environment. This dual-triggered oxygen self-supply nanoplatform can ensure both photosensitizing and self-supported oxygen for sustained and improved PDT (Fig. 9a). In a similar study, Rhodamine B (RhB) en-

capsulated manganese dioxide (MnO_2) was assembled onto polypeptide-functionalized BP, in which R- MnO_2 acted as an O_2 supplier in the presence of H_2O_2 [311] (Fig. 9b). Moreover, the Mn^{2+} and RhB dyes released from the nanocomposites can achieve a real-time fluorescence/MRI dual-mode imaging. As a typical example, this design strategy can effectively resolve the hypoxic issue and thus shows great potential in the treatment of hypoxia-related diseases.

AM has also been used as a PDT agent for cancer noninvasive therapy owing to its good stability for phototherapy (Fig. 10). In a recent study, AM NPs shielded with the cell membrane (CmNPs) showed remarkably good biostability and enhanced PTC efficacy [130]. As compared with traditional AM nanosheets, CmNPs also revealed superior tumor-targeting ability and thus achieved excellent PA/photothermal multi-modal imaging at tumor sites. *In vivo* study showed that the tumor in the 4T1 tumor-bearing mice subjected to CmNPs nanocomposites was eliminated without notable side effects. Despite the huge potential of AM-based nanomaterials for multimodal therapy, the research on the application of AM and other Xenes for cancer therapy is scarce. Hence, more relevant work should be strengthened in the future.

Transition metal dichalcogenides

MoS_2 -based nanocomposites and other TMDs have also found their utilization as photosensitizers for PDT applications [312]. Han and co-workers [313] reported a multifunctional nanoplatform with good stability and biocompatibility on the basis of MoS_2 nanosheets-chitosan (CS) complex. The MoS_2 -CS was covalently decorated with UCNPs for upconversion luminescence and FA for tumor-targeting purposes, followed by the

Figure 9 (a) Schematic for the preparation of BP-based dual-triggered oxygen self-supply nanoplatforms (Cy5-dHeme-BPNS-FA) for enhanced PDT and illustration of their intracellular actions in the body. Reprinted with permission from Ref. [310], Copyright 2018, Elsevier Ltd. (b) Schematic illustration of synthesis of R- MnO_2 -FBP and the mechanism of self-supply oxygen for enhanced PDT. Reprinted with permission from Ref. [311], Copyright 2018, Elsevier Ltd.

Figure 10 Schematic illustration of the preparation of AM-based NPs (CmNP) and for multimodality imaging-guided PDT/PTT. Reprinted with permission from Ref. [130], Copyright 2019, the Royal Society of Chemistry.

loading of the photosensitizer phthalocyanine (ZnPc) to achieve synergistic PDT/PTT. The injection of this MoS₂-based nanoplatform into the breast tumor model caused significant inhibition of tumor growth and also induced tumor death, especially when exposed to NIR laser irradiation. Besides the combination with organic molecules/polymers, doping with other metallic nanomaterial/NPs can also be applied to construct high-cellular-uptake and specific delivery system. Liu *et al.* [314] reported a MoS₂-based nanocomposite combining with gold NPs, to achieve synergistic cancer treatment including PTT, PDT, and CT imaging. It was highlighted that the hyperthermia effect induced by this MoS₂-based nanocomposite could enhance PDT efficacy by boosting blood flow and supplying more oxygen molecules.

MoS₂ QDs have also been exploited for PDT. According to Li *et al.* [315], MoS₂-QDs can be grafted onto mesoporous silica *via* a disulfide bond to prepare a nanoplatform for a combined PTT/PDT. Furthermore, the obtained MoS₂@ss-SiO₂ was immobilized with HA for tumor-targeting and Ce6 as photosensitizer (Fig. 11). This design of MoS₂@ss-SiO₂ can distinctly enlarge the diameter of MoS₂@ss-SiO₂-based nanoplatform for tumor targeting and eliminate the toxicity from MoS₂ nanomaterials. Similar to MoS₂ QDs, WS₂ nanodots have been

observed to exert the photodynamic effect, proved by Wang *et al.* [316] *via* the combination of WS₂ nanodots with HA, PANI, and Ce6 to realize a multi-modality therapy including PTT, PDT and radiation. As PDT requires sufficient oxygen supply in the tumor micro-environment, the initial PTT hyperthermia effect caused by the WS₂ nanodots under NIR laser irradiation can significantly accelerate blood flow and improve oxygen supply in tumor sites, leading to improved therapeutic efficacy.

MXene

Ti₃C₂ MXene has been proposed to be a novel and efficient photosensitizer that can effectively produce ROS under NIR irradiation, due to the outstanding mass extinction coefficient (28.6 L g⁻¹ cm⁻¹ under irradiation) and high PTC efficiency (~58.3%) [317], and has been proved for a combination treatment of PDT/PTT. The inert surface of Ti₃C₂ can be further modified or loaded with DOX *via* non-covalent interactions such as π - π stacking and electrostatic interactions. Nevertheless, the utilization of MXene for PDT application is scarce, and thus more relevant research needs to be carried out. Meanwhile, their biosafety and biocompatibility also need to be further studied.

Figure 11 (a) Schematic for synthesis of $\text{MoS}_2\text{@ss-SiO}_2\text{-Ce6/HA}$ nanocomposites and its mechanisms for multimodal imaging-guided PTT and PDT. Reprinted with permission from Ref. [315], Copyright 2019, American Chemical Society.

Other types of 2D nanomaterials

The excellent anionic exchanging and acid sensitivity properties of 2D LDH can be exploited to develop tumor microenvironment (TME)-responsive nanocarriers for the loading of photosensitizers and antitumor drugs. Photosensitizers such as Ce6 [318], methylene blue (MB) [273] and ICG [274] have been reported to be incorporated with pH-sensitive LDH-based nanomaterials for MRI or fluorescence imaging-guided PDT. In the research reported by Li *et al.* [319], pH-responsive zinc(II) phthalocyanine-containing octasulfonate (ZnPcS_8) doped LDH (LDH-ZnPcS_8) was prepared by a simple coprecipitation method. *In vitro* study in the HepG2 cell line demonstrated a stronger photodynamic activity of the obtained LDH-ZnPcS_8 than that of ZnPcS_8 alone. Later, several researchers demonstrated the integration of the O_2 -evolving system with LDH-based photosensitizers to improve PDT efficiency. Ruan *et al.* [273] developed a FeMn-LDH nanocarrier to load photosensitizer MB for PDT. Due to the catalase-like activity of FeMn-LDH , the as-designed nanoplatform could overcome tumor hypoxia by catalyzing H_2O_2 to produce O_2 , thus enhancing the ROS generation of the photosensitizer. In this study, FeMn-LDH has been also noted to exert a photothermal effect, and thus FeMn-LDH/MB

could be a promising nanoplatform for PTT-PDT synergistic therapy. In another recent study, CoMn -doped LDH (CoMn-LDH), which was capable of TME targeting and decomposing H_2O_2 into O_2 , was used as a photosensitizer nanocarrier for PDT [320]. After loading Ce6, the obtained nanocomposite showed remarkable ROS production under 650 nm irradiation, and significantly enhanced the performance of both PAI and MRI.

Lin's group [321] first reported the study of MOF for PDT in 2014, in which an Hf-porphyrin nMOF was synthesized for *in vivo* treatment of head and neck cancer. Lately, Shi *et al.* [322] demonstrated the integration of UCNPs, meso-tetra(4-carboxyphenyl)porphine (TCPP)-MOF and ultrasmall TiO_2 NPs for achieving Type I and Type II PDT. As expected, this nanoplatform can significantly induce cancer cell apoptosis *in vitro* and *in vivo*. Compositional and structural tunability of nMOF can also improve the effectiveness of PDT by ameliorating tumor hypoxia and avoiding the aggregation of photosensitizers such as Ce6. For example, Wang and co-workers [323] synthesized an Mn-based mesoporous manganese cobalt oxide derived from $\text{Mn}_3[\text{Co}(\text{CN})_6]_2$, and this mesoporous nano-enzyme was further loaded with Ce6 to increase the local O_2 concentration by decomposing intracellular H_2O_2 by Mn ions. The combi-

nation of photodynamic nMOFs with other types of therapy such as PTT, gene therapy and immunotherapy has also been developed, to enhance the therapy efficacy [324–326].

Sonodynamic therapy

SDT has gained increasing attention for tumor treatment in recent years. Analogous to PDT requiring the assis-

tance of photosensitizers, SDT needs the involvement of additional ultrasound-sensitive agents, normally known as sonosensitizers to be activated under ultrasound irradiation for ROS generation to kill cancer cells [327,328]. Besides, the collapse of ultrasound cavitation microbubbles can cause the generation of strong shock waves, which could contribute to localized high temperature and high pressure from the sonosensitizers to improve the

Table 2 Summary of various 2D nanomaterials for PDT and SDT applications

Therapeutic platform	2D nanomaterials	<i>In vitro</i>	<i>In vivo</i>	Therapy strategy	Ref.
NGO-mPEG/ZnPc	NGO	MCF-7 breast cancer cell line	–	PDT	[295]
NGP-AIE	NGO	UMUC3 cell line	UMUC3 tumor xenograft model	PDT	[299]
chit-rGO-IR820-DOX	rGO	CT26 cell line	–	PDT, PTT, chemotherapy	[300]
UCNs-GOQDs-FA/TPP	GOQDs	HeLa cells	HeLa tumor model	PDT	[302]
PC@GCPD(Gd)	GQDs	EMT6 cell line	EMT6 tumor-bearing mice	PDT, PTT, chemotherapy	[303]
BP nanosheets	BP nanosheets	MDA-MB-231 cell line	Xenograft tumor model	PDT	[114]
PEGylated BPQDs	BPQDs	HeLa cell or L02 cell line	S180 tumor bearing mice model	PDT	[351]
PEGylated BPQDs	BPQDs	Hep G2 cells	4T1 tumor-bearing Balb/c mice	PDT, PTT	[228]
R-MnO ₂ -FBP	BP nanosheets	HeLa cells	HeLa tumor model	PDT	[311]
Cy5-dHeme-BPNS-FA	BP nanosheets	HeLa cells	HeLa tumor model	PDT	[310]
MnO ₂ -UCNPs-FA/ZnPc	MoS ₂ nanosheet	MDA-MB-231/ HCC38/ MCF-7 cells	HCC38 orthotopic triple-negative breast tumor model	PTT, PDT	[313]
PEG-MnO ₂ -Au-Ce6	MoS ₂ nanosheet	4T1 cells	4T1 tumor-bearing mice	PTT, PDT	[314]
MnO ₂ @ss-SiO ₂ -Ce6/HA	MoS ₂ nanodots	4T1 cells	4T1-tumor-bearing mice	PTT, PDT	[315]
HA-WS ₂ @PANI/Ce6	WS ₂ nanodots	4T1 cells	4T1 tumor-bearing nude mice	PTT, PDT, RT	[316]
Ti ₃ C ₂ -DOX	Ti ₃ C ₂ nanosheets	HCT-116 and A2780 cell line	Tumor bearing mice	PDT, PTT, chemotherapy	[317]
CmNP	AM nanosheets	4T1 cells	4T1-xenografted mice	PTT, PDT	[130]
LDH-ZnPcS ₈	LDH	HepG2 cell line	H22 tumor-bearing mice	PDT	[319]
FeMn-LDH/MB	LDH	HeLa cells	HeLa-tumor-bearing nude mice	PDT/PTT	[273]
Ce6/CoMn-LDH	LDH	HeLa cells	HeLa-tumor-bearing nude mice	PDT/CDT	[320]
nrGO@MSN-ION-PEG-RB	rGO	SKBr3 cells	SKBr3 tumor bearing nude mice	SDT	[341]
MnO _x /TiO ₂ -GR-PVP	rGO	4T1 cells	4T1-tumor-bearing mice	SDT	[342]
HAu-TiO ₂ NCs	Au	SCC7 cells	SCC7 tumor-bearing mice	SDT	[345]
Au NPL@TiO ₂	Au nanoplate	HeLa cells	HeLa-tumor-bearing nude mice	SDT	[346]
Au@BP	BP nanosheets	4T1 cells	4T1-tumor-bearing mice	SDT	[350]

therapy efficacy [329]. Table 2 shows the recent achievements of 2D nanomaterials in PDT and SDT fields. Although operated in a similar principle to PDT, SDT has the extra advantage of treating deep region cancer cells [330], while PDT technique suffers from the poor tissue penetration of the excitation light (just mm scale) [331]. Thus, SDT has been recognized as a real-time monitoring and high-resolution approach for non-invasive treatment without depth limitation [332,333].

Most of the sonosensitizers are traditional organic molecules that are originally utilized as photosensitizers such as protoporphyrin IX, hematoporphyrin monomethyl ether (HMME), and ATX-70. Similar to their utilization in PDT, these sonosensitizers of SDT have the same shortcomings such as low biocompatibility and phototoxicity [334]. The emerging nano-technologies can address these limitations and improve the SDT efficacy, since nanomaterials possess several distinct advantages including the ease of modification, the facile preparation procedure, and the convenient tailoring of their properties such as hydrophobicity and biocompatibility [335,336]. Moreover, the combination of emerging nanotechnologies with sonosensitizers and photosensitizers is supposed to produce multi-modalities in a single nanoplatform for cancer treatment [337,338].

Owing to their good electrical and thermal conductivity, graphene-related materials have been studied as heat-conducting bases for elevating local temperature under ultrasound irradiation, which is expected to cause deep directional hyperthermia for cancer therapy as well as realize synergistic therapeutic effects of SDT and hyperthermia therapy [339,340]. Chen *et al.* [341] synthesized an rGO-based transonic hybrid that can be triggered by low-power focus ultrasound (FUS) condition for cancer SDT/hyperthermia therapy: the rGO nanosheets were firstly loaded with MSN-iron-oxide NPs (IONs) for SDT enhancement and hyperthermia therapy under FUS irradiation, followed by decoration with Rose Bengal (RB) as a sonosensitizer. *In vivo* study revealed highly synergistic effects of SDT and FUS hyperthermia, and thus a significant suppression of tumor growth was achieved even for those in the deep region.

rGO possesses high electroconductivity and therefore can be used for effective separation of the electron (e^-) and hole (h^+) pairs from the energy band as generated by the ultrasonic irradiation-induced cavitation effect. This capacity of rGO can be exploited to enhance the ROS generation of sonosensitizers. Dai *et al.* [342] demonstrated the combination of rGO with titanium dioxide (TiO_2) for enhanced SDT. It was noted that the TiO_2 -rGO

nanocomposites exhibit a higher tumor inhibition rate as compared with the use of TiO_2 -PEG nanoplatform. This remarkable suppression ability is mainly ascribed to the improvement of ROS generation in the presence of rGO, due to its excellent electroconductivity and high PTC capability.

Au and Ag NPs are also noted to improve the quantum yield of ROS generation of TiO_2 NPs by effectively separating the electron (e^-) and hole (h^+) [343,344]. Deepagan *et al.* [345] reported combined Au- TiO_2 nanocomposites ($\text{HAu-TiO}_2\text{NCs}$), the ROS generation capability of which was evaluated *in vitro* using diphenylisobenzofuran (DPBF). It was noted that the amount of ROS generated from the combined nanocomposites was higher than that of hydrophilic TiO_2 -NPs, i.e., in the absence of 2D Au NPs. Recently, Gao *et al.* [346] reported a 2D gold nanoplates (NPLs) cloaked with TiO_2 shell as synergetic cancer therapeutic agents for combined PTT/SDT (Fig. 12). The ROS generation was significantly enhanced in Au NPL@ TiO_2 nanostructures group compared with that of pure TiO_2 NPs under ultrasonic irradiation, due to the high PTC efficiency of Au NPL@ TiO_2 nanostructures (up to 42.05%) under 1064 nm laser irradiation. Therefore, a significant anti-tumor efficacy based on this 2D metal-hybrid nanostructure was achieved.

As noted above, 2D metallic nanomaterials, e.g., TiO_2 , are always subjected to the low yield of $^1\text{O}_2$ generation and unsatisfactory bio-distribution effects, which is mainly ascribed to the short electron-hole separation [347,348]. In recent years, organic nanomaterials as so-

Figure 12 Schematic of preparing Au NPL@ TiO_2 nanostructures for PTT/SDT against HeLa cells. Reprinted with permission from Ref. [346], Copyright 2019, the Royal Society of Chemistry.

Figure 13 (a, b) Preparation of Au@BP nanohybrids for SDT-based cancer treatment under ultrasound irradiation. (c) The ROS production percentages of Au@BP nanohybrids under 660 nm NIR or ultrasound irradiation with/without pork skin screening. Reprinted with permission from Ref. [350], Copyright 2018, the Royal Society of Chemistry.

nosensitizer agents for SDT have also been explored for overcoming these limitations. It is known that BP possesses unique electronic and optical properties, which contribute to its potential use as singlet oxygen generators for cancer treatment, although the detailed mechanism is still unclear [349]. Inspired by this, Ouyang *et al.* [350] firstly demonstrated that BP nanosheets were served as a sonosensitizer to combine with Au-NPs for SDT (Fig. 13a, b). These Au@BP nanohybrids showed higher efficiency of ¹O₂ production than that of single Au-NPs when exposed to ultrasound irradiation. In addition, the ¹O₂ production in the presence of nanohybrids under the action of ultrasound was 4.7 times higher than under 660 nm irradiation alone (Fig. 13c). Biological experiments revealed significant inhibition of tumor growth with little side effects. This work demonstrates that 2D organic nanosheets are very prospective in the SDT application and could be effective alternatives for metallic nanosensitizers.

CONCLUSIONS AND OUTLOOK

In this work, we thoroughly summarized the promising applications of NIR/ultrasound-sensitive 2D nanomaterials for cancer therapy. Owing to their unique mechanical, physical and chemical properties including high PTC efficiency, and high surface-to-volume ratios, these 2D nano-materials have been exploited as excellent nanocarriers or photosensitizer/sonosensitizer agents, showing huge potential for PTT, PDT, SDT or multimodal therapy. The development of graphene family, BP and TMDs

have been extensively investigated for cancer treatment in recent years, while the research on the biomedical application of other Xenes, GDY, and h-BN is still at a start-up stage. Therefore, it is suggested that relevant investigation should be strengthened in the future. Despite the prominence of these nanomaterials in the field of non-invasive approaches, there are still several issues that have to be overcome prior to clinical translation.

From the perspective of nanomaterial preparation, the size of nanoplateforms, water solubility/wettability, and their dimension are determining factors for their subsequent biological performances. Thus, these fabrication parameters need to be optimized towards precisely controlling the nanomaterial dimensions and morphologies, tailoring their surface properties and renovating their functions. Currently, there still lack standard protocols to synthesize most of the 2D materials with uniform size and thickness, although the bottom-up approaches show huge potentials to overcome some of the key challenges in the preparation aspect. Besides, some nanomaterials suffer from rapid degradation and poor stability, e.g., BP and AM, and thus it is necessary to develop new methods to further improve their stability [352,353]. Also, the interactions between these nanomaterials with exogenous drugs or agents are still poorly understood, which is critical for fabricating a new nanocarrier system and further improving the loading capacity of external agents. A better understanding of such knowledge will also help to comprehend how these nanomaterials will interact with biological molecules, e.g., proteins or DNA in human bodies. This is of critical importance in terms of

reducing their toxicity and eliminating the side effects [354].

From the biomedical point of view, most of the current investigations are carried out by using mouse models *via* injection manner to local tumor sites, but this administration method limits the wide use of these nanocomposites, especially for the therapy of tumors in the deep bio-tissue, which is still one major challenge in the clinical trial. Given these, the improvement of administration method, e.g., developing effective oral drug/intravenous-injection agents is a key challenge for any nanomaterial-based platform. SDT shows more promising than PTT and PDT in treating tumors in the deep location, owing to its intrinsic characteristics; nevertheless, the exploration of nanomaterials in the SDT field still stays at a preliminary stage and more efforts will be needed for its development. The 2D nanoplateforms have made great progress to achieve multimodal co-therapy, giving rise to synergistic effects for cancer therapy. Cellular metabolism of the nanoplateforms is of great importance to improve their therapeutic efficacy. Nevertheless, little knowledge is known in this area, e.g., the details of the synergistic mechanism, and the clearance time in bodies. The ligand/antibody-mediated NPs are always engulfed by cells *via* endocytosis to form early endosome, and therefore the endosome escape is crucial to achieving the drug delivery especially the gene delivery. The design of smart delivery systems based on degradable 2D-nanomaterials combining with stimuli-responsive nanomaterials could potentially overcome this challenge [355]. For example, BP can fast degrade under acidic endosome, and the resulting phosphite/phosphate ion could elevate osmotic pressure to facilitate endosomal escape [356].

In addition, some of those multimodal functions could be not clinically relevant, despite the ingenious design strategies applied. The researchers in the materials science are supposed to seek cooperation with the clinical researchers, and thus more efforts could be dedicated to resolving the key problems in clinical trials. Drug factors, administration manner, dosing and delivery times, etc. are common concerns in the design and development of nanomedicine. However, these seem overlooked in current biomedical research of 2D nanomaterials for cancer therapy. The translation opportunity of these nanomaterials into clinical nanomedicine will arise, when biomedical engineers take them into consideration in their research.

The ‘nanotoxicology’ has emerged as a new discipline in recent years [357,358]. Despite the low toxicity of the

abovementioned nanomaterials, their side effects and toxicity are not systematically investigated and poorly elucidated, e.g., some studies have reported that the use of BP nanosheets in large sizes or at high concentrations ($50\text{ }\mu\text{g mL}^{-1}$) can induce notable cytotoxicity [112,113]. The toxicity of 2D materials is a double-edged sword since they could be also toxic to tumor cells or viruses. Hence, based on a suitable modulation and functionalization to reduce the damage to normal tissues, the toxic nanomaterials could be used for cancer treatment with a synergistic antitumor effect. Typical examples are that the metallic NPs, such as silver and iron oxide, exhibit significant antibacterial and antitumor properties [359,360]. From this point, some metal-based 2D materials, e.g., TMD, could have similar functions, which is worthy to be further investigated.

Whereas the promise of 2D nanomaterials for non-invasive cancer therapy seems to be within reach, the concern of bio-safety remains a big issue of nanomaterials. Few of the current nanomaterials have reached clinical research or translation. One related concern is that whether these nanomaterials with excellent PTC effects and good biocompatibility would facilitate cancer cell metastasis. As it is well-known that nanomaterials have the advantage of overcoming the biological barrier and can reach different tissues with blood circulation. This concern has been proved by one recent study that NPs promote breast cancer cell intravasation and extravasation by inducing endothelial leakiness [358]. Therefore, a systematic investigation of the nanoplateforms’ pharmacokinetics is needed in future work. In addition, the fabrication of tumor-responsive or microenvironment-degradable nanoplateform might be an effective strategy to overcome the bio-safety concern in terms of cancer therapy. Lastly, more fundamental studies of these nanodrugs on renal and hepatic metabolism will be required, since the NPs tend to aggregate in these tissues, leading to inflammatory response or serve abnormalities. A better understanding of the metabolism of these nanomaterials will help to guide us in overcoming these biosafety barriers.

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- 1 Ferlay J, Colombet M, Soerjomataram I, *et al.* Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *Eur J Cancer*, 2018, 103: 356–387
- 2 Hiller JG, Perry NJ, Poulgiannis G, *et al.* Perioperative events influence cancer recurrence risk after surgery. *Nat Rev Clin Oncol*, 2018, 15: 205–218
- 3 Shibue T, Weinberg RA. EMT, CSCs, and drug resistance: The

- mechanistic link and clinical implications. *Nat Rev Clin Oncol*, 2017, 14: 611–629
- 4 Wu Y, Xu G, Jin X, *et al.* Supramolecular dendritic polymers for diagnostic and theranostic applications. *Sci China Mater*, 2018, 61: 1444–1453
- 5 Mohammad-Hadi L, MacRobert AJ, Loizidou M, *et al.* Photodynamic therapy in 3D cancer models and the utilisation of nanodelivery systems. *Nanoscale*, 2018, 10: 1570–1581
- 6 Canavese G, Ancona A, Racca L, *et al.* Nanoparticle-assisted ultrasound: A special focus on sonodynamic therapy against cancer. *Chem Eng J*, 2018, 340: 155–172
- 7 Li X, Lee S, Yoon J. Supramolecular photosensitizers rejuvenate photodynamic therapy. *Chem Soc Rev*, 2018, 47: 1174–1188
- 8 Luby BM, Walsh CD, Zheng G. Advanced photosensitizer activation strategies for smarter photodynamic therapy beacons. *Angew Chem Int Ed*, 2019, 58: 2558–2569
- 9 Wang L, Hu Y, Hao Y, *et al.* Tumor-targeting core-shell structured nanoparticles for drug procedural controlled release and cancer sonodynamic combined therapy. *J Control Release*, 2018, 286: 74–84
- 10 Sun T, Zhang G, Wang Q, *et al.* A targeting theranostics nanomedicine as an alternative approach for hyperthermia perfusion. *Biomaterials*, 2018, 183: 268–279
- 11 Guo X, Wei X, Chen Z, *et al.* Multifunctional nanoplateforms for subcellular delivery of drugs in cancer therapy. *Prog Mater Sci*, 2020, 107: 100599
- 12 Shi J, Kantoff PW, Wooster R, *et al.* Cancer nanomedicine: Progress, challenges and opportunities. *Nat Rev Cancer*, 2017, 17: 20–37
- 13 Fan T, Zhou Y, Qiu M, *et al.* Black phosphorus: A novel nanoplateform with potential in the field of bio-photonic nanomedicine. *J Innov Opt Health Sci*, 2018, 11: 1830003
- 14 Ji X, Kong N, Wang J, *et al.* A novel top-down synthesis of ultrathin 2D boron nanosheets for multimodal imaging-guided cancer therapy. *Adv Mater*, 2018, 30: 1803031
- 15 Iannazzo D, Ziccarelli I, Pistone A. Graphene quantum dots: Multifunctional nanoplateforms for anticancer therapy. *J Mater Chem B*, 2017, 5: 6471–6489
- 16 Liu J, Jiang X, Zhang R, *et al.* MXene-enabled electrochemical microfluidic biosensor: Applications toward multicomponent continuous monitoring in whole blood. *Adv Funct Mater*, 2018, 29: 1807326
- 17 Bao Q, Zhang H, Ni Z, *et al.* Monolayer graphene as a saturable absorber in a mode-locked laser. *Nano Res*, 2010, 4: 297–307
- 18 Bao Q, Zhang H, Wang B, *et al.* Broadband graphene polarizer. *Nat Photon*, 2011, 5: 411–415
- 19 Huang H, Ren X, Li Z, *et al.* Two-dimensional bismuth nanosheets as prospective photo-detector with tunable optoelectronic performance. *Nanotechnology*, 2018, 29: 235201
- 20 Zhang H, Tang D, Knize RJ, *et al.* Graphene mode locked, wavelength-tunable, dissipative soliton fiber laser. *Appl Phys Lett*, 2010, 96: 111112
- 21 Fan T, Xie Z, Huang W, *et al.* Two-dimensional non-layered selenium nanoflakes: Facile fabrications and applications for self-powered photo-detector. *Nanotechnology*, 2019, 30: 114002
- 22 Ge Y, Zhu Z, Xu Y, *et al.* Broadband nonlinear photoresponse of 2D TiS₂ for ultrashort pulse generation and all-optical thresholding devices. *Adv Opt Mater*, 2018, 6: 1701166
- 23 Jiang X, Gross S, Withford MJ, *et al.* Low-dimensional nanomaterial saturable absorbers for ultrashort-pulsed waveguide lasers. *Opt Mater Express*, 2018, 8: 3055–3071
- 24 Jiang X, Liu S, Liang W, *et al.* Broadband nonlinear photonics in few-layer MXene Ti₃C₂T_x (T=F, O, or OH). *Laser Photon Rev*, 2018, 12: 1700229
- 25 Dhanabalan SC, Ponraj JS, Zhang H, *et al.* Present perspectives of broadband photodetectors based on nanobelts, nanoribbons, nanosheets and the emerging 2D materials. *Nanoscale*, 2016, 8: 6410–6434
- 26 Qi X, Zhang Y, Ou Q, *et al.* Photonics and optoelectronics of 2D metal-halide perovskites. *Small*, 2018, 14: 1800682
- 27 Wang Z, Xu Y, Dhanabalan SC, *et al.* Black phosphorus quantum dots as an efficient saturable absorber for bound soliton operation in an erbium doped fiber laser. *IEEE Photonics J*, 2016, 8: 1–10
- 28 Huang W, Xie Z, Fan T, *et al.* Black-phosphorus-analogue tin monosulfide: An emerging optoelectronic two-dimensional material for high-performance photodetection with improved stability under ambient/harsh conditions. *J Mater Chem C*, 2018, 6: 9582–9593
- 29 Lu S, Ge Y, Sun Z, *et al.* Ultrafast nonlinear absorption and nonlinear refraction in few-layer oxidized black phosphorus. *Photon Res*, 2016, 4: 286–292
- 30 Luo S, Zhao J, Zou J, *et al.* Self-standing polypyrrole/black phosphorus laminated film: Promising electrode for flexible supercapacitor with enhanced capacitance and cycling stability. *ACS Appl Mater Interfaces*, 2018, 10: 3538–3548
- 31 Chen L, Chen C, Chen W, *et al.* Biodegradable black phosphorus nanosheets mediate specific delivery of hTERT siRNA for synergistic cancer therapy. *ACS Appl Mater Interfaces*, 2018, 10: 21137–21148
- 32 Yu B, Goel S, Ni D, *et al.* Reassembly of ⁸⁹Zr-labeled cancer cell membranes into multicompartiment membrane-derived liposomes for PET-trackable tumor-targeted theranostics. *Adv Mater*, 2018, 30: 1704934
- 33 Li Z, Chen Y, Yang Y, *et al.* Recent advances in nanomaterials-based chemo-photothermal combination therapy for improving cancer treatment. *Front Bioeng Biotechnol*, 2019, 7: 293
- 34 Madamsetty VS, Mukherjee A, Mukherjee S. Recent trends of the bio-inspired nanoparticles in cancer theranostics. *Front Pharmacol*, 2019, 10: 1264
- 35 Stubelius A, Lee S, Almutairi A. The chemistry of boronic acids in nanomaterials for drug delivery. *Acc Chem Res*, 2019, 52: 3108–3119
- 36 Liu L, Yao H, Li H, *et al.* Recent advances of low-dimensional materials in lasing applications. *FlatChem*, 2018, 10: 22–38
- 37 Tang Q, Zhou Z. Graphene-analogous low-dimensional materials. *Prog Mater Sci*, 2013, 58: 1244–1315
- 38 Zhang H, Wang J, Hasan T, *et al.* Photonics of 2D materials. *Opt Commun*, 2018, 406: 1–2
- 39 Liu Y, Li J, Chen H, *et al.* Magnet-activatable nanoliposomes as intracellular bubble microreactors to enhance drug delivery efficacy and burst cancer cells. *Nanoscale*, 2019, 11: 18854–18865
- 40 Liu X, Guo Q, Qiu J. Emerging low-dimensional materials for nonlinear optics and ultrafast photonics. *Adv Mater*, 2017, 29: 1605886
- 41 Men L, White MA, Andaraarachchi H, *et al.* Synthetic development of low dimensional materials. *Chem Mater*, 2016, 29: 168–175
- 42 Lennon T, Bakewell D, Willis E. Workplace lactation support in milwaukee county 5 years after the affordable care act. *J Hum Lact*, 2017, 33: 214–219

- 43 Chimene D, Alge DL, Gaharwar AK. Two-dimensional nanomaterials for biomedical applications: Emerging trends and future prospects. *Adv Mater*, 2015, 27: 7261–7284
- 44 Broza YY, Vishinkin R, Barash O, *et al.* Synergy between nanomaterials and volatile organic compounds for non-invasive medical evaluation. *Chem Soc Rev*, 2018, 47: 4781–4859
- 45 Pasinszki T, Krebsz M, Tung TT, *et al.* Carbon nanomaterial based biosensors for non-invasive detection of cancer and disease biomarkers for clinical diagnosis. *Sensors*, 2017, 17: 1919
- 46 Tripathi KM, Kim TY, Losic D, *et al.* Recent advances in engineered graphene and composites for detection of volatile organic compounds (VOCs) and non-invasive diseases diagnosis. *Carbon*, 2016, 110: 97–129
- 47 Shi L, Zhao T. Recent advances in inorganic 2D materials and their applications in lithium and sodium batteries. *J Mater Chem A*, 2017, 5: 3735–3758
- 48 Huang C, Li Y, Wang N, *et al.* Progress in research into 2D graphdiyne-based materials. *Chem Rev*, 2018, 118: 7744–7803
- 49 Singh D, Gupta SK, Sonvane Y, *et al.* Antimonene: A monolayer material for ultraviolet optical nanodevices. *J Mater Chem C*, 2016, 4: 6386–6390
- 50 Bao Q, Zhang H, Wang Y, *et al.* Atomic-layer graphene as a saturable absorber for ultrafast pulsed lasers. *Adv Funct Mater*, 2009, 19: 3077–3083
- 51 Huang Z, Han W, Tang H, *et al.* Photoelectrochemical-type sunlight photodetector based on MoS₂/graphene heterostructure. *2D Mater*, 2015, 2: 035011
- 52 Jiang Y, Miao L, Jiang G, *et al.* Broadband and enhanced non-linear optical response of MoS₂/graphene nanocomposites for ultrafast photonics applications. *Sci Rep*, 2015, 5: 16372
- 53 Wang H, Miao L, Jiang Y, *et al.* Enhancing the saturable absorption and carrier dynamics of graphene with plasmonic nanowires. *Phys Status Solidi B*, 2015, 252: 2159–2166
- 54 Zhang H, Tang D, Zhao L, *et al.* Vector dissipative solitons in graphene mode locked fiber lasers. *Opt Commun*, 2010, 283: 3334–3338
- 55 Kravets VG, Grigorenko AN, Nair RR, *et al.* Spectroscopic ellipsometry of graphene and an exciton-shifted van Hove peak in absorption. *Phys Rev B*, 2010, 81: 155413
- 56 Miao L, Jiang Y, Lu S, *et al.* Broadband ultrafast nonlinear optical response of few-layers graphene: Toward the mid-infrared regime. *Photon Res*, 2015, 3: 214–219
- 57 Yin F, Gu B, Lin Y, *et al.* Functionalized 2D nanomaterials for gene delivery applications. *Coord Chem Rev*, 2017, 347: 77–97
- 58 Liu Y, Duan X, Huang Y, *et al.* Two-dimensional transistors beyond graphene and TMDCs. *Chem Soc Rev*, 2018, 47: 6388–6409
- 59 Liu X, Ma D, Tang H, *et al.* Polyamidoamine dendrimer and oleic acid-functionalized graphene as biocompatible and efficient gene delivery vectors. *ACS Appl Mater Interfaces*, 2014, 6: 8173–8183
- 60 Russier J, León V, Orecchioni M, *et al.* Few-layer graphene kills selectively tumor cells from myelomonocytic leukemia patients. *Angew Chem Int Ed*, 2017, 56: 3014–3019
- 61 Lu J, Cheng C, He YS, *et al.* Multilayered graphene hydrogel membranes for guided bone regeneration. *Adv Mater*, 2016, 28: 4025–4031
- 62 Zeng S, Sreekanth KV, Shang J, *et al.* Graphene-gold metasurface architectures for ultrasensitive plasmonic biosensing. *Adv Mater*, 2015, 27: 6163–6169
- 63 McCallion C, Burthem J, Rees-Unwin K, *et al.* Graphene in therapeutics delivery: Problems, solutions and future opportunities. *Eur J Pharm BioPharm*, 2016, 104: 235–250
- 64 Yang K, Zhang S, Zhang G, *et al.* Graphene in mice: Ultrahigh *in vivo* tumor uptake and efficient photothermal therapy. *Nano Lett*, 2010, 10: 3318–3323
- 65 Yin T, Liu J, Zhao Z, *et al.* Redox sensitive hyaluronic acid-decorated graphene oxide for photothermally controlled tumor-cytoplasm-selective rapid drug delivery. *Adv Funct Mater*, 2017, 27: 1604620
- 66 Ruan J, Wang X, Yu Z, *et al.* Enhanced physiochemical and mechanical performance of chitosan-grafted graphene oxide for superior osteoinductivity. *Adv Funct Mater*, 2016, 26: 1085–1097
- 67 Cheeewattanagul N, Morales-Narváez E, Hassan ARHA, *et al.* Straightforward immunosensing platform based on graphene oxide-decorated nanopaper: A highly sensitive and fast biosensing approach. *Adv Funct Mater*, 2017, 27: 1702741
- 68 Reina G, González-Domínguez JM, Criado A, *et al.* Promises, facts and challenges for graphene in biomedical applications. *Chem Soc Rev*, 2017, 46: 4400–4416
- 69 Yan M, Liu Y, Zhu X, *et al.* Nanoscale reduced graphene oxide-mediated photothermal therapy together with IDO inhibition and PD-L1 blockade synergistically promote antitumor immunity. *ACS Appl Mater Interfaces*, 2019, 11: 1876–1885
- 70 He L, Sarkar S, Barras A, *et al.* Electrochemically stimulated drug release from flexible electrodes coated electrophoretically with doxorubicin loaded reduced graphene oxide. *Chem Commun*, 2017, 53: 4022–4025
- 71 Huo D, Liu G, Li Y, *et al.* Construction of antithrombotic tissue-engineered blood vessel *via* reduced graphene oxide based dual-enzyme biomimetic cascade. *ACS Nano*, 2017, 11: 10964–10973
- 72 Povedano E, Cincotto FH, Parrado C, *et al.* Decoration of reduced graphene oxide with rhodium nanoparticles for the design of a sensitive electrochemical enzyme biosensor for 17 β -estradiol. *Biosens Bioelectron*, 2017, 89: 343–351
- 73 Bitounis D, Ali-Boucetta H, Hong BH, *et al.* Prospects and challenges of graphene in biomedical applications. *Adv Mater*, 2013, 25: 2258–2268
- 74 Cheng C, Li S, Thomas A, *et al.* Functional graphene nanomaterials based architectures: Biointeractions, fabrications, and emerging biological applications. *Chem Rev*, 2017, 117: 1826–1914
- 75 Li G, Li Y, Liu H, *et al.* Architecture of graphdiyne nanoscale films. *Chem Commun*, 2010, 46: 3256–3258
- 76 Tang H, Hessel CM, Wang J, *et al.* Two-dimensional carbon leading to new photoconversion processes. *Chem Soc Rev*, 2014, 43: 4281–4299
- 77 Chang F, Huang L, Li Y, *et al.* A short review of synthesis of graphdiyne and its potential applications. *Int J Electrochem Sci*, 2017, 12: 10348–10358
- 78 Zhou J, Xie Z, Liu R, *et al.* Synthesis of ultrathin graphdiyne film using a surface template. *ACS Appl Mater Interfaces*, 2019, 11: 2632–2637
- 79 Qian X, Ning Z, Li Y, *et al.* Construction of graphdiyne nanowires with high-conductivity and mobility. *Dalton Trans*, 2012, 41: 730–733
- 80 Li G, Li Y, Qian X, *et al.* Construction of tubular molecule aggregations of graphdiyne for highly efficient field emission. *J Phys Chem C*, 2011, 115: 2611–2615
- 81 Prabakaran P, Satapathy S, Prasad E, *et al.* Architecting pyridiine nanowalls with improved inter-molecular interactions, electronic

- features and transport characteristics. *J Mater Chem C*, 2018, 6: 380–387
- 82 Wang SS, Liu HB, Kan XN, *et al.* Superlyophilicity-facilitated synthesis reaction at the microscale: Ordered graphdiyne stripe arrays. *Small*, 2017, 13: 1602265
- 83 Sharma A, Wen B, Liu B, *et al.* Defect engineering in few-layer phosphorene. *Small*, 2018, 14: 1704556
- 84 Van den Heuvel W, Soncini A. Dirac cones in the spectrum of bond-decorated graphenes. *J Chem Phys*, 2014, 140: 234114
- 85 Deb J, Bhattacharya B, Singh NB, *et al.* First principle study of adsorption of boron-halogenated system on pristine graphyne. *Struct Chem*, 2016, 27: 1221–1227
- 86 Chen X, Fang D, Zhang Y, *et al.* Novel electronic transport of zigzag graphdiyne nanoribbons induced by edge states. *Europhys Lett*, 2014, 107: 57002
- 87 Mehran S, Rouhi S, Salmalian K. Molecular dynamics simulations of the adsorption of polymer chains on graphyne and its family. *Physica B-Condensed Matter*, 2015, 456: 41–49
- 88 Nagarajan V, Chandiramouli R. Investigation of NH₃ adsorption behavior on graphdiyne nanosheet and nanotubes: A first-principles study. *J Mol Liq*, 2018, 249: 24–32
- 89 Qiu H, Sheng X. A first principle study of hydrogenated graphdiyne. *Phys Lett A*, 2018, 382: 662–666
- 90 Enyashin AN, Ivanovskii AL. Fluorographynes: Stability, structural and electronic properties. *Superlattices MicroStruct*, 2013, 55: 75–82
- 91 Yan Z, Wang L, Cheng J, *et al.* Lithium-decorated oxidized graphyne for hydrogen storage by first principles study. *J Appl Phys*, 2014, 116: 174304
- 92 Gao X, Zhou J, Du R, *et al.* Robust superhydrophobic foam: A graphdiyne-based hierarchical architecture for oil/water separation. *Adv Mater*, 2016, 28: 168–173
- 93 Liu J, Chen C, Zhao Y. Progress and prospects of graphdiyne-based materials in biomedical applications. *Adv Mater*, 2019, 31: 1804386
- 94 Li S, Chen Y, Liu H, *et al.* Graphdiyne materials as nano-transducer for *in vivo* photoacoustic imaging and photothermal therapy of tumor. *Chem Mater*, 2017, 29: 6087–6094
- 95 Jin J, Guo M, Liu J, *et al.* Graphdiyne nanosheet-based drug delivery platform for photothermal/chemotherapy combination treatment of cancer. *ACS Appl Mater Interfaces*, 2018, 10: 8436–8442
- 96 Tran V, Soklaski R, Liang Y, *et al.* Layer-controlled band gap and anisotropic excitons in few-layer black phosphorus. *Phys Rev B*, 2014, 89: 235319
- 97 Woome AH, Farnsworth TW, Hu J, *et al.* Phosphorene: Synthesis, scale-up, and quantitative optical spectroscopy. *ACS Nano*, 2015, 9: 8869–8884
- 98 Ou H, Li J, Chen C, *et al.* Organic/polymer photothermal nanoagents for photoacoustic imaging and photothermal therapy *in vivo*. *Sci China Mater*, 2019, 62: 1740–1758
- 99 Kong L, Qin Z, Xie G, *et al.* Black phosphorus as broadband saturable absorber for pulsed lasers from 1 μm to 2.7 μm wavelength. *Laser Phys Lett*, 2016, 13: 045801
- 100 Li C, Liu J, Guo Z, *et al.* Black phosphorus saturable absorber for a diode-pumped passively Q-switched Er:CaF₂ mid-infrared laser. *Opt Commun*, 2018, 406: 158–162
- 101 Buscema M, Groenendijk DJ, Blanter SI, *et al.* Fast and broadband photoresponse of few-layer black phosphorus field-effect transistors. *Nano Lett*, 2014, 14: 3347–3352
- 102 Han C, Hu Z, Gomes LC, *et al.* Surface functionalization of black phosphorus via potassium toward high-performance complementary devices. *Nano Lett*, 2017, 17: 4122–4129
- 103 Wood JD, Wells SA, Jariwala D, *et al.* Effective passivation of exfoliated black phosphorus transistors against ambient degradation. *Nano Lett*, 2014, 14: 6964–6970
- 104 Qin Z, Xie G, Zhang H, *et al.* Black phosphorus as saturable absorber for the Q-switched Er:ZBLAN fiber laser at 28 μm . *Opt Express*, 2015, 23: 24713–24718
- 105 Chu Z, Liu J, Guo Z, *et al.* 2 μm passively Q-switched laser based on black phosphorus. *Opt Mater Express*, 2016, 6: 2374–2379
- 106 Chen X, Xu G, Ren X, *et al.* A black/red phosphorus hybrid as an electrode material for high-performance Li-ion batteries and supercapacitors. *J Mater Chem A*, 2017, 5: 6581–6588
- 107 Ramireddy T, Xing T, Rahman MM, *et al.* Phosphorus-carbon nanocomposite anodes for lithium-ion and sodium-ion batteries. *J Mater Chem A*, 2015, 3: 5572–5584
- 108 Xu GL, Chen Z, Zhong GM, *et al.* Nanostructured black phosphorus/Ketjenblack-multiwalled carbon nanotubes composite as high performance anode material for sodium-ion batteries. *Nano Lett*, 2016, 16: 3955–3965
- 109 Liu H, Tao L, Zhang Y, *et al.* Bridging covalently functionalized black phosphorus on graphene for high-performance sodium-ion battery. *ACS Appl Mater Interfaces*, 2017, 9: 36849–36856
- 110 Haghighat-Shishavan S, Nazarian-Samani M, Nazarian-Samani M, *et al.* Strong, persistent superficial oxidation-assisted chemical bonding of black phosphorus with multiwall carbon nanotubes for high-capacity ultradurable storage of lithium and sodium. *J Mater Chem A*, 2018, 6: 10121–10134
- 111 Qiu M, Singh A, Wang D, *et al.* Biocompatible and biodegradable inorganic nanostructures for nanomedicine: Silicon and black phosphorus. *Nano Today*, 2019, 25: 135–155
- 112 Latiff NM, Teo WZ, Sofer Z, *et al.* The cytotoxicity of layered black phosphorus. *Chem Eur J*, 2015, 21: 13991–13995
- 113 Zhang X, Zhang Z, Zhang S, *et al.* Size effect on the cytotoxicity of layered black phosphorus and underlying mechanisms. *Small*, 2017, 13: 1701210
- 114 Wang H, Yang X, Shao W, *et al.* Ultrathin black phosphorus nanosheets for efficient singlet oxygen generation. *J Am Chem Soc*, 2015, 137: 11376–11382
- 115 Majoral JP, François JM, Fabre R, *et al.* Multiplexing technology for *in vitro* diagnosis of pathogens: The key contribution of phosphorus dendrimers. *Sci China Mater*, 2018, 61: 1454–1461
- 116 Yin F, Hu K, Chen S, *et al.* Black phosphorus quantum dot based novel siRNA delivery systems in human pluripotent teratoma PA-1 cells. *J Mater Chem B*, 2017, 5: 5433–5440
- 117 Sun Z, Zhao Y, Li Z, *et al.* TiL₄-coordinated black phosphorus quantum dots as an efficient contrast agent for *in vivo* photoacoustic imaging of cancer. *Small*, 2017, 13: 1602896
- 118 Fojtů M, Chia X, Sofer Z, *et al.* Black phosphorus nanoparticles potentiate the anticancer effect of oxaliplatin in ovarian cancer cell line. *Adv Funct Mater*, 2017, 27: 1701955
- 119 Zhao Y, Tong L, Li Z, *et al.* Stable and multifunctional dye-modified black phosphorus nanosheets for near-infrared imaging-guided photothermal therapy. *Chem Mater*, 2017, 29: 7131–7139
- 120 Tao W, Ji X, Xu X, *et al.* Antimonene quantum dots: Synthesis and application as near-infrared photothermal agents for effective cancer therapy. *Angew Chem Int Ed*, 2017, 56: 11896–11900
- 121 Zhang S, Xie M, Li F, *et al.* Semiconducting group 15 monolayers:

- A broad range of band gaps and high carrier mobilities. *Angew Chem Int Ed*, 2016, 55: 1666–1669
- 122 Pumera M, Sofer Z. 2D monoelemental arsenene, antimonene, and bismuthene: Beyond black phosphorus. *Adv Mater*, 2017, 29: 1605299
 - 123 Wang L, Xu D, Gao J, *et al.* Semiconducting quantum dots: Modification and applications in biomedical science. *Sci China Mater*, 2020, 63: 1631–1650
 - 124 Ares P, Aguilar-Galindo F, Rodríguez-San-Miguel D, *et al.* Mechanical isolation of highly stable antimonene under ambient conditions. *Adv Mater*, 2016, 28: 6332–6336
 - 125 Gibaja C, Rodríguez-San-Miguel D, Ares P, *et al.* Few-layer antimonene by liquid-phase exfoliation. *Angew Chem Int Ed*, 2016, 55: 14345–14349
 - 126 Ares P, Palacios JJ, Abellán G, *et al.* Recent progress on antimonene: A new bidimensional material. *Adv Mater*, 2018, 30: 1703771
 - 127 Wang X, He J, Zhou B, *et al.* Bandgap-tunable preparation of smooth and large two-dimensional antimonene. *Angew Chem Int Ed*, 2018, 57: 8668–8673
 - 128 Wang X, Song J, Qu J. Antimonene: From experimental preparation to practical application. *Angew Chem Int Ed*, 2019, 58: 1574–1584
 - 129 Tao W, Ji X, Zhu X, *et al.* Two-dimensional antimonene-based photonic nanomedicine for cancer theranostics. *Adv Mater*, 2018, 30: 1802061
 - 130 Lu G, Lv C, Bao W, *et al.* Antimonene with two-orders-of-magnitude improved stability for high-performance cancer theranostics. *Chem Sci*, 2019, 10: 4847–4853
 - 131 Guan G, Zhang S, Liu S, *et al.* Protein induces layer-by-layer exfoliation of transition metal dichalcogenides. *J Am Chem Soc*, 2015, 137: 6152–6155
 - 132 Li H, Wu J, Yin Z, *et al.* Preparation and applications of mechanically exfoliated single-layer and multilayer MoS₂ and WS₂ nanosheets. *Acc Chem Res*, 2014, 47: 1067–1075
 - 133 Joensen P, Frindt RF, Morrison SR. Single-layer MoS₂. *Mater Res Bull*, 1986, 21: 457–461
 - 134 Yuwen L, Yu H, Yang X, *et al.* Rapid preparation of single-layer transition metal dichalcogenide nanosheets *via* ultrasonication enhanced lithium intercalation. *Chem Commun*, 2016, 52: 529–532
 - 135 Novoselov KS, Jiang D, Schedin F, *et al.* Two-dimensional atomic crystals. *Proc Natl Acad Sci USA*, 2005, 102: 10451–10453
 - 136 Benavente E. Intercalation chemistry of molybdenum disulfide. *Coord Chem Rev*, 2002, 224: 87–109
 - 137 Daeneke T, Clark RM, Carey BJ, *et al.* Reductive exfoliation of substoichiometric MoS₂ bilayers using hydrazine salts. *Nanoscale*, 2016, 8: 15252–15261
 - 138 O'Neill A, Khan U, Coleman JN. Preparation of high concentration dispersions of exfoliated MoS₂ with increased flake size. *Chem Mater*, 2012, 24: 2414–2421
 - 139 Li X, Shan J, Zhang W, *et al.* Recent advances in synthesis and biomedical applications of two-dimensional transition metal dichalcogenide nanosheets. *Small*, 2017, 13: 1602660
 - 140 Rao CNR, Ramakrishna Matte HSS, Maitra U. Graphene analogues of inorganic layered materials. *Angew Chem Int Ed*, 2013, 52: 13162–13185
 - 141 Zhang X, Lai Z, Tan C, *et al.* Solution-processed two-dimensional MoS₂ nanosheets: Preparation, hybridization, and applications. *Angew Chem Int Ed*, 2016, 55: 8816–8838
 - 142 Lu X, Utama MIB, Lin J, *et al.* Large-area synthesis of monolayer and few-layer MoSe₂ films on SiO₂ substrates. *Nano Lett*, 2014, 14: 2419–2425
 - 143 Manzeli S, Ovchinnikov D, Pasquier D, *et al.* 2D transition metal dichalcogenides. *Nat Rev Mater*, 2017, 2: 17033
 - 144 Jariwala D, Sangwan VK, Lauhon LJ, *et al.* Emerging device applications for semiconducting two-dimensional transition metal dichalcogenides. *ACS Nano*, 2014, 8: 1102–1120
 - 145 Mak KF, Shan J. Photonics and optoelectronics of 2D semiconductor transition metal dichalcogenides. *Nat Photon*, 2016, 10: 216–226
 - 146 Chen H, Liu T, Su Z, *et al.* 2D transition metal dichalcogenide nanosheets for photo/thermo-based tumor imaging and therapy. *Nanoscale Horiz*, 2018, 3: 74–89
 - 147 Lei Z, Zhu W, Xu S, *et al.* Hydrophilic MoSe₂ nanosheets as effective photothermal therapy agents and their application in smart devices. *ACS Appl Mater Interfaces*, 2016, 8: 20900–20908
 - 148 Zhang C, Hu DF, Xu JW, *et al.* Polyphenol-assisted exfoliation of transition metal dichalcogenides into nanosheets as photothermal nanocarriers for enhanced antibiofilm activity. *ACS Nano*, 2018, 12: 12347–12356
 - 149 Urbanová V, Pumera M. Biomedical and bioimaging applications of 2D pnictogens and transition metal dichalcogenides. *Nanoscale*, 2019, 11: 15770–15782
 - 150 Zhang A, Li A, Zhao W, *et al.* Recent advances in functional polymer decorated two-dimensional transition-metal dichalcogenides nanomaterials for chemo-photothermal therapy. *Chem Eur J*, 2018, 24: 4215–4227
 - 151 Naguib M, Kurtoglu M, Presser V, *et al.* Two-dimensional nanocrystals produced by exfoliation of Ti₃AlC₂. *Adv Mater*, 2011, 23: 4248–4253
 - 152 Szuplewska A, Kulpińska D, Dybko A, *et al.* 2D Ti₂C (MXene) as a novel highly efficient and selective agent for photothermal therapy. *Mater Sci Eng-C*, 2019, 98: 874–886
 - 153 Lin H, Gao S, Dai C, *et al.* 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
 - 154 Han X, Huang J, Lin H, *et al.* 2D ultrathin MXene-based drug-delivery nanoplatform for synergistic photothermal ablation and chemotherapy of cancer. *Adv Healthc Mater*, 2018, 7: 1701394
 - 155 Li Z, Zhang H, Han J, *et al.* Surface nanopore engineering of 2D MXenes for targeted and synergistic multitherapies of hepatocellular carcinoma. *Adv Mater*, 2018, 30: 1706981
 - 156 Liu Z, Zhao M, Lin H, *et al.* 2D magnetic titanium carbide MXene for cancer theranostics. *J Mater Chem B*, 2018, 6: 3541–3548
 - 157 Lin H, Chen Y, Shi J. Insights into 2D MXenes for versatile biomedical applications: Current advances and challenges ahead. *Adv Sci*, 2018, 5: 1800518
 - 158 Zhang C, Li Y, Zhang P, *et al.* Antimonene quantum dot-based solid-state solar cells with enhanced performance and high stability. *Sol Energy Mater Sol Cells*, 2019, 189: 11–20
 - 159 Tay RY, Park HJ, Ryu GH, *et al.* Synthesis of aligned symmetrical multifaceted monolayer hexagonal boron nitride single crystals on resolidified copper. *Nanoscale*, 2016, 8: 2434–2444
 - 160 Zhi C, Hanagata N, Bando Y, *et al.* Dispersible shortened boron nitride nanotubes with improved molecule-loading capacity. *Chem Asian J*, 2011, 6: 2530–2535
 - 161 Sainsbury T, Satti A, May P, *et al.* Oxygen radical functionalization of boron nitride nanosheets. *J Am Chem Soc*, 2012, 134:

- 18758–18771
- 162 Wang W, Bando Y, Zhi C, *et al.* Aqueous noncovalent functionalization and controlled near-surface carbon doping of multi-walled boron nitride nanotubes. *J Am Chem Soc*, 2008, 130: 8144–8145
- 163 Maguer A, Leroy E, Bresson L, *et al.* A versatile strategy for the functionalization of boron nitride nanotubes. *J Mater Chem*, 2009, 19: 1271–1275
- 164 Chen X, Wu P, Rousseas M, *et al.* Boron nitride nanotubes are noncytotoxic and can be functionalized for interaction with proteins and cells. *J Am Chem Soc*, 2009, 131: 890–891
- 165 Lahiri D, Rouzaud F, Richard T, *et al.* Boron nitride nanotube reinforced polylactide-polycaprolactone copolymer composite: Mechanical properties and cytocompatibility with osteoblasts and macrophages *in vitro*. *Acta Biomater*, 2010, 6: 3524–3533
- 166 Li L, Li LH, Ramakrishnan S, *et al.* Controlling wettability of boron nitride nanotube films and improved cell proliferation. *J Phys Chem C*, 2012, 116: 18334–18339
- 167 Ciofani G, Danti S, Genchi GG, *et al.* Boron nitride nanotubes: Biocompatibility and potential spill-over in nanomedicine. *Small*, 2013, 9: 1672–1685
- 168 Shanmugam V, Selvakumar S, Yeh CS. Near-infrared light-responsive nanomaterials in cancer therapeutics. *Chem Soc Rev*, 2014, 43: 6254–6287
- 169 Liu Y, Bhattarai P, Dai Z, *et al.* Photothermal therapy and photoacoustic imaging *via* nanotheranostics in fighting cancer. *Chem Soc Rev*, 2019, 48: 2053–2108
- 170 Farokhi M, Mottaghitab F, Saeb MR, *et al.* Functionalized theranostic nanocarriers with bio-inspired polydopamine for tumor imaging and chemo-photothermal therapy. *J Control Release*, 2019, 309: 203–219
- 171 Day E, Fay B, Melamed J. Nanoshell-mediated photothermal therapy can enhance chemotherapy in inflammatory breast cancer cells. *Int J Nanomed*, 2015, 10: 6931–6941
- 172 Kong L, Xing L, Zhou B, *et al.* Dendrimer-modified MoS₂ nanoflakes as a platform for combinational gene silencing and photothermal therapy of tumors. *ACS Appl Mater Interfaces*, 2017, 9: 15995–16005
- 173 Wang BK, Yu XF, Wang JH, *et al.* Gold-nanorods-siRNA nanoplex for improved photothermal therapy by gene silencing. *Biomaterials*, 2015, 78: 27–39
- 174 Wei P, Chen J, Hu Y, *et al.* Dendrimer-stabilized gold nanostars as a multifunctional theranostic nanoplatform for CT imaging, photothermal therapy, and gene silencing of tumors. *Adv Healthc Mater*, 2017, 5: 3203–3213
- 175 Hou X, Tao Y, Pang Y, *et al.* Nanoparticle-based photothermal and photodynamic immunotherapy for tumor treatment. *Int J Cancer*, 2018, 143: 3050–3060
- 176 Li L, Yang S, Song L, *et al.* An endogenous vaccine based on fluorophores and multivalent immunoadjuvants regulates tumor micro-environment for synergistic photothermal and immunotherapy. *Theranostics*, 2018, 8: 860–873
- 177 Zhou B, Song J, Wang M, *et al.* BSA-bioinspired gold nanorods loaded with immunoadjuvant for the treatment of melanoma by combined photothermal therapy and immunotherapy. *Nanoscale*, 2018, 10: 21640–21647
- 178 Jung HS, Verwilt P, Sharma A, *et al.* Organic molecule-based photothermal agents: An expanding photothermal therapy universe. *Chem Soc Rev*, 2018, 47: 2280–2297
- 179 Bao Z, Liu X, Liu Y, *et al.* Near-infrared light-responsive inorganic nanomaterials for photothermal therapy. *Asian J Pharm Sci*, 2016, 11: 349–364
- 180 Murugan C, Sharma V, Murugan RK, *et al.* Two-dimensional cancer theranostic nanomaterials: Synthesis, surface functionalization and applications in photothermal therapy. *J Control Release*, 2019, 299: 1–20
- 181 Li Z, Huang H, Tang S, *et al.* Small gold nanorods laden macrophages for enhanced tumor coverage in photothermal therapy. *Biomaterials*, 2016, 74: 144–154
- 182 Bao X, Ou Q, Xu ZQ, *et al.* Band structure engineering in 2D materials for optoelectronic applications. *Adv Mater Technol*, 2018, 3: 1800072
- 183 de Melo-Diogo D, Lima-Sousa R, Alves CG, *et al.* Graphene family nanomaterials for application in cancer combination photothermal therapy. *Biomater Sci*, 2019, 7: 3534–3551
- 184 Yao J, Wang H, Chen M, *et al.* Recent advances in graphene-based nanomaterials: Properties, toxicity and applications in chemistry, biology and medicine. *Microchim Acta*, 2019, 186: 395
- 185 Chen YW, Su YL, Hu SH, *et al.* Functionalized graphene nanocomposites for enhancing photothermal therapy in tumor treatment. *Adv Drug Deliver Rev*, 2016, 105: 190–204
- 186 Schaaf L, Schwab M, Ulmer C, *et al.* Hyperthermia synergizes with chemotherapy by inhibiting PARP1-dependent DNA replication arrest. *Cancer Res*, 2016, 76: 2868–2875
- 187 Mahmood M, Karmakar A, Fejleh A, *et al.* Synergistic enhancement of cancer therapy using a combination of carbon nanotubes and anti-tumor drug. *Nanomedicine*, 2009, 4: 883–893
- 188 Li X, Zhang Y, Ma Z, *et al.* The fabrication of rGO/(PLL/PASP)₃@DOX nanorods with pH-switch for photothermal therapy and chemotherapy. *Chem Eur J*, 2018, 24: 13830–13838
- 189 Su T, Cheng F, Yan J, *et al.* Hierarchical nanocomposites of graphene oxide and PEGylated protoporphyrin as carriers to load doxorubicin hydrochloride for trimodal synergistic therapy. *J Mater Chem B*, 2018, 6: 4687–4696
- 190 Chong Y, Ma Y, Shen H, *et al.* The *in vitro* and *in vivo* toxicity of graphene quantum dots. *Biomaterials*, 2014, 35: 5041–5048
- 191 Yao X, Niu X, Ma K, *et al.* Graphene quantum dots-capped magnetic mesoporous silica nanoparticles as a multifunctional platform for controlled drug delivery, magnetic hyperthermia, and photothermal therapy. *Small*, 2017, 13: 1602225
- 192 Yang C, Chan KK, Xu G, *et al.* Biodegradable polymer-coated multifunctional graphene quantum dots for light-triggered synergistic therapy of pancreatic cancer. *ACS Appl Mater Interfaces*, 2019, 11: 2768–2781
- 193 Qian R, Maiti D, Zhong J, *et al.* Multifunctional nano-graphene based nanocomposites for multimodal imaging guided combined radioisotope therapy and chemotherapy. *Carbon*, 2019, 149: 55–62
- 194 Chang X, Zhang Y, Xu P, *et al.* Graphene oxide/MnWO₄ nanocomposite for magnetic resonance/photoacoustic dual-modal imaging and tumor photothermo-chemotherapy. *Carbon*, 2018, 138: 397–409
- 195 Xuan Y, Zhang RY, Zhao DH, *et al.* Ultrafast synthesis of gold nanosphere cluster coated by graphene quantum dot for active targeting PA/CT imaging and near-infrared laser/pH-triggered chemo-photothermal synergistic tumor therapy. *Chem Eng J*, 2019, 369: 87–99
- 196 Srimathi U, Nagarajan V, Chandiramouli R. Investigation on graphdiyne nanosheet in adsorption of sorafenib and regorafenib drugs: A DFT approach. *J Mol Liq*, 2019, 277: 776–785

- 197 Jiang W, Zhang Z, Wang Q, *et al.* Tumor reoxygenation and blood perfusion enhanced photodynamic therapy using ultrathin graphdiyne oxide nanosheets. *Nano Lett*, 2019, 19: 4060–4067
- 198 Robinson JT, Tabakman SM, Liang Y, *et al.* Ultrasmall reduced graphene oxide with high near-infrared absorbance for photothermal therapy. *J Am Chem Soc*, 2011, 133: 6825–6831
- 199 Sun Z, Xie H, Tang S, *et al.* Ultrasmall black phosphorus quantum dots: Synthesis and use as photothermal agents. *Angew Chem Int Ed*, 2015, 54: 11526–11530
- 200 Hessel CM, P. Pattani V, Rasch M, *et al.* Copper selenide nanocrystals for photothermal therapy. *Nano Lett*, 2011, 11: 2560–2566
- 201 Tian Q, Jiang F, Zou R, *et al.* Hydrophilic Cu₂S₃ nanocrystals: A photothermal agent with a 25.7% heat conversion efficiency for photothermal ablation of cancer cells *in vivo*. *ACS Nano*, 2011, 5: 9761–9771
- 202 Tyagi N, Attia NF, Geckeler KE. Exfoliated graphene nanosheets: pH-sensitive drug carrier and anti-cancer activity. *J Colloid Interface Sci*, 2017, 498: 364–377
- 203 Xie J, Wang N, Dong X, *et al.* Graphdiyne nanoparticles with high free radical scavenging activity for radiation protection. *ACS Appl Mater Interfaces*, 2019, 11: 2579–2590
- 204 Li J, Luo H, Zhai B, *et al.* Black phosphorus: A two-dimension saturable absorption material for mid-infrared Q-switched and mode-locked fiber lasers. *Sci Rep*, 2016, 6: 30361
- 205 Wang HD, Sang DK, Guo ZN, *et al.* Black phosphorus-based field effect transistor devices for Ag ions detection. *Chin Phys B*, 2018, 27: 087308
- 206 Mu H, Lin S, Wang Z, *et al.* Black phosphorus-polymer composites for pulsed lasers. *Adv Opt Mater*, 2015, 3: 1447–1453
- 207 Jiang Q, Xu L, Chen N, *et al.* Facile synthesis of black phosphorus: An efficient electrocatalyst for the oxygen evolving reaction. *Angew Chem Int Ed*, 2016, 55: 13849–13853
- 208 Qiu M, Sun ZT, Sang DK, *et al.* Current progress in black phosphorus materials and their applications in electrochemical energy storage. *Nanoscale*, 2017, 9: 13384–13403
- 209 Ren X, Li Z, Huang Z, *et al.* Environmentally robust black phosphorus nanosheets in solution: Application for self-powered photodetector. *Adv Funct Mater*, 2017, 27: 1606834
- 210 Wu L, Xie Z, Lu L, *et al.* Few-layer tin sulfide: A promising black-phosphorus-analogue 2D material with exceptionally large non-linear optical response, high stability, and applications in all-optical switching and wavelength conversion. *Adv Opt Mater*, 2018, 6: 1700985
- 211 Guo Z, Zhang H, Lu S, *et al.* From black phosphorus to phosphorene: Basic solvent exfoliation, evolution of Raman scattering, and applications to ultrafast photonics. *Adv Funct Mater*, 2015, 25: 6996–7002
- 212 Lu SB, Miao LL, Guo ZN, *et al.* Broadband nonlinear optical response in multi-layer black phosphorus: An emerging infrared and mid-infrared optical material. *Opt Express*, 2015, 23: 11183–11194
- 213 Zhou J, Li Z, Ying M, *et al.* Black phosphorus nanosheets for rapid microRNA detection. *Nanoscale*, 2018, 10: 5060–5064
- 214 Qian X, Gu Z, Chen Y. Two-dimensional black phosphorus nanosheets for theranostic nanomedicine. *Mater Horiz*, 2017, 4: 800–816
- 215 Shao J, Xie H, Huang H, *et al.* Biodegradable black phosphorus-based nanospheres for *in vivo* photothermal cancer therapy. *Nat Commun*, 2016, 7: 12967
- 216 Yang G, Wan X, Gu Z, *et al.* Near infrared photothermal-responsive poly(vinyl alcohol)/black phosphorus composite hydrogels with excellent on-demand drug release capacity. *J Mater Chem B*, 2018, 6: 1622–1632
- 217 Tao W, Zhu X, Yu X, *et al.* Black phosphorus nanosheets as a robust delivery platform for cancer theranostics. *Adv Mater*, 2017, 29: 1603276
- 218 Wu F, Zhang M, Chu X, *et al.* Black phosphorus nanosheets-based nanocarriers for enhancing chemotherapy drug sensitivity via depleting mutant p53 and resistant cancer multimodal therapy. *Chem Eng J*, 2019, 370: 387–399
- 219 Deng L, Xu Y, Sun C, *et al.* Functionalization of small black phosphorus nanoparticles for targeted imaging and photothermal therapy of cancer. *Sci Bull*, 2018, 63: 917–924
- 220 Yang X, Wang D, Shi Y, *et al.* Black phosphorus nanosheets immobilizing Ce6 for imaging-guided photothermal/photodynamic cancer therapy. *ACS Appl Mater Interfaces*, 2018, 10: 12431–12440
- 221 Lee H, Dellatore SM, Miller WM, *et al.* Mussel-inspired surface chemistry for multifunctional coatings. *Science*, 2007, 318: 426–430
- 222 Lyu Q, Hsueh N, Chai CLL. The chemistry of bioinspired catechol (amine)-based coatings. *ACS Biomater Sci Eng*, 2019, 5: 2708–2724
- 223 Li Z, Xu H, Shao J, *et al.* Polydopamine-functionalized black phosphorus quantum dots for cancer theranostics. *Appl Mater Today*, 2019, 15: 297–304
- 224 Lyu Q, Hsueh N, Chai CLL. Unravelling the polydopamine mystery: Is the end in sight? *Polym Chem*, 2019, 10: 5771–5777
- 225 Lyu Q, Hsueh N, Chai CLL. Direct evidence for the critical role of 5,6-dihydroxyindole in polydopamine deposition and aggregation. *Langmuir*, 2019, 35: 5191–5201
- 226 Zeng X, Luo M, Liu G, *et al.* Polydopamine-modified black phosphorous nanocapsule with enhanced stability and photothermal performance for tumor multimodal treatments. *Adv Sci*, 2018, 5: 1800510
- 227 Zhang M, Wang W, Wu F, *et al.* Black phosphorus quantum dots gated, carbon-coated Fe₃O₄ nanocapsules (BPQDs@ss-Fe₃O₄@C) with low premature release could enable imaging-guided cancer combination therapy. *Chem Eur J*, 2018, 24: 12890–12901
- 228 Li Y, Liu Z, Hou Y, *et al.* Multifunctional nanoplatform based on black phosphorus quantum dots for bioimaging and photodynamic/photothermal synergistic cancer therapy. *ACS Appl Mater Interfaces*, 2017, 9: 25098–25106
- 229 Liang X, Ye X, Wang C, *et al.* Photothermal cancer immunotherapy by erythrocyte membrane-coated black phosphorus formulation. *J Control Release*, 2019, 296: 150–161
- 230 Xu Y, Wang Z, Guo Z, *et al.* Solvothermal synthesis and ultrafast photonics of black phosphorus quantum dots. *Adv Opt Mater*, 2016, 4: 1223–1229
- 231 Wang S, Shao J, Li Z, *et al.* Black phosphorus-based multimodal nanoagent: Showing targeted combinatory therapeutics against cancer metastasis. *Nano Lett*, 2019, 19: 5587–5594
- 232 Luo M, Cheng W, Zeng X, *et al.* Folic acid-functionalized black phosphorus quantum dots for targeted chemo-photothermal combination cancer therapy. *Pharmaceutics*, 2019, 11: 242
- 233 Zheng T, Zhou T, Feng X, *et al.* Enhanced plasmon-induced resonance energy transfer (PIRET)-mediated photothermal and photodynamic therapy guided by photoacoustic and magnetic resonance imaging. *ACS Appl Mater Interfaces*, 2019, 11: 31615–

- 31626
- 234 Xue T, Liang W, Li Y, *et al.* Ultrasensitive detection of miRNA with an antimonene-based surface plasmon resonance sensor. *Nat Commun*, 2019, 10: 28
- 235 Niu X, Li Y, Zhang Y, *et al.* Greatly enhanced photoabsorption and photothermal conversion of antimonene quantum dots through spontaneously partial oxidation. *ACS Appl Mater Interfaces*, 2019, 11: 17987–17993
- 236 Yu J, Wang XH, Feng J, *et al.* Antimonene nanoflakes: Extraordinary photoacoustic performance for high-contrast imaging of small volume tumors. *Adv Healthc Mater*, 2019, 8: 1900378
- 237 Eftekhari A. Tungsten dichalcogenides (WS_2 , WSe_2 , and WTe_2): Materials chemistry and applications. *J Mater Chem A*, 2017, 5: 18299–18325
- 238 Yadav V, Roy S, Singh P, *et al.* 2D MoS_2 -based nanomaterials for therapeutic, bioimaging, and biosensing applications. *Small*, 2019, 15: 1803706
- 239 Wang H, Naghadeh SB, Li C, *et al.* Enhanced photoelectrochemical and photocatalytic activities of CdS nanowires by surface modification with MoS_2 nanosheets. *Sci China Mater*, 2018, 61: 839–850
- 240 Gong L, Yan L, Zhou R, *et al.* Two-dimensional transition metal dichalcogenide nanomaterials for combination cancer therapy. *J Mater Chem B*, 2017, 5: 1873–1895
- 241 Ponraj JS, Xu ZQ, Dhanabalan SC, *et al.* Photonics and optoelectronics of two-dimensional materials beyond graphene. *Nanotechnology*, 2016, 27: 462001
- 242 Chen L, Feng W, Zhou X, *et al.* Facile synthesis of novel albumin-functionalized flower-like MoS_2 nanoparticles for *in vitro* chemophotothermal synergistic therapy. *RSC Adv*, 2016, 6: 13040–13049
- 243 Liu T, Wang C, Cui W, *et al.* Combined photothermal and photodynamic therapy delivered by PEGylated MoS_2 nanosheets. *Nanoscale*, 2014, 6: 11219–11225
- 244 Liu J, Li F, Zheng J, *et al.* Redox/NIR dual-responsive MoS_2 for synergistic chemo-photothermal therapy of cancer. *J Nanobiotechnol*, 2019, 17: 78
- 245 Meng X, Liu Z, Cao Y, *et al.* Fabricating aptamer-conjugated PEGylated- $MoS_2/Cu_1.8S$ theranostic nanoplatform for multiplexed imaging diagnosis and chemo-photothermal therapy of cancer. *Adv Funct Mater*, 2017, 27: 1605592
- 246 Geng B, Qin H, Zheng F, *et al.* Carbon dot-sensitized MoS_2 nanosheet heterojunctions as highly efficient NIR photothermal agents for complete tumor ablation at an ultralow laser exposure. *Nanoscale*, 2019, 11: 7209–7220
- 247 Xu S, Li D, Wu P. One-pot, facile, and versatile synthesis of monolayer MoS_2/WS_2 quantum dots as bioimaging probes and efficient electrocatalysts for hydrogen evolution reaction. *Adv Funct Mater*, 2015, 25: 1127–1136
- 248 Wang J, Tan X, Pang X, *et al.* MoS_2 quantum dot@polyaniline inorganic-organic nanohybrids for *in vivo* dual-modal imaging guided synergistic photothermal/radiation therapy. *ACS Appl Mater Interfaces*, 2016, 8: 24331–24338
- 249 Zhang A, Li A, Zhao W, *et al.* An efficient and self-guided chemophotothermal drug loading system based on copolymer and transferrin decorated MoS_2 nanodots for dually controlled drug release. *Chem Eng J*, 2018, 342: 120–132
- 250 Song X, Shang W, Peng L, *et al.* Novel GPC3-binding WS_2-Ga^{3+} -PEG-peptide nanosheets for *in vivo* bimodal imaging-guided photothermal therapy. *Nanomedicine*, 2018, 13: 1681–1693
- 251 Yang G, Zhang R, Liang C, *et al.* Manganese dioxide coated $WS_2@Fe_3O_4/sSiO_2$ nanocomposites for pH-responsive MR imaging and oxygen-elevated synergetic therapy. *Small*, 2018, 14: 1702664
- 252 Wu C, Wang S, Zhao J, *et al.* Biodegradable Fe(III)@ WS_2 -PVP nanocapsules for redox reaction and TME-enhanced nanocatalytic, photothermal, and chemotherapy. *Adv Funct Mater*, 2019, 29: 1901722
- 253 Wang Y, Zhao J, Chen Z, *et al.* Construct of $MoSe_2/Bi_2Se_3$ nanoheterostructure: Multimodal CT/PT imaging-guided PTT/PDT/chemotherapy for cancer treating. *Biomaterials*, 2019, 217: 119282
- 254 Xie H, Li Z, Sun Z, *et al.* Metabolizable ultrathin Bi_2Se_3 nanosheets in imaging-guided photothermal therapy. *Small*, 2016, 12: 4136–4145
- 255 Sun L, Hou M, Zhang L, *et al.* PEGylated mesoporous Bi_2S_3 nanostars loaded with chlorin e6 and doxorubicin for fluorescence/CT imaging-guided multimodal therapy of cancer. *Nanomed-Nanotechnol Biol Med*, 2019, 17: 1–12
- 256 Bai J, Jia X, Ruan Y, *et al.* Photosensitizer-conjugated Bi_2Te_3 nanosheets as theranostic agent for synergistic photothermal and photodynamic therapy. *Inorg Chem*, 2018, 57: 10180–10188
- 257 Xia Y, Qian D, Hsieh D, *et al.* Observation of a large-gap topological-insulator class with a single dirac cone on the surface. *Nat Phys*, 2009, 5: 398–402
- 258 Li J, Jiang F, Yang B, *et al.* Topological insulator bismuth selenide as a theranostic platform for simultaneous cancer imaging and therapy. *Sci Rep*, 2013, 3: 1998
- 259 Cheng L, Shen S, Shi S, *et al.* $FeSe_2$ -decorated Bi_2Se_3 nanosheets fabricated *via* cation exchange for chelator-free ^{64}Cu -labeling and multimodal image-guided photothermal-radiation therapy. *Adv Funct Mater*, 2016, 26: 2185–2197
- 260 Du J, Gu Z, Yan L, *et al.* Poly(vinylpyrrolidone)- and selenocysteine-modified Bi_2Se_3 nanoparticles enhance radiotherapy efficacy in tumors and promote radioprotection in normal tissues. *Adv Mater*, 2017, 29: 1701268
- 261 Shao J, Xie H, Wang H, *et al.* 2D material-based nanofibrous membrane for photothermal cancer therapy. *ACS Appl Mater Interfaces*, 2018, 10: 1155–1163
- 262 Dai C, Lin H, Xu G, *et al.* Biocompatible 2D titanium carbide (MXenes) composite nanosheets for pH-responsive MRI-guided tumor hyperthermia. *Chem Mater*, 2017, 29: 8637–8652
- 263 Huang K, Li Z, Lin J, *et al.* Two-dimensional transition metal carbides and nitrides (MXenes) for biomedical applications. *Chem Soc Rev*, 2018, 47: 5109–5124
- 264 Lin H, Wang X, Yu L, *et al.* Two-dimensional ultrathin MXene ceramic nanosheets for photothermal conversion. *Nano Lett*, 2017, 17: 384–391
- 265 Xing C, Chen S, Liang X, *et al.* Two-dimensional MXene (Ti_3C_2)-integrated cellulose hydrogels: Toward smart three-dimensional network nanoplatfroms exhibiting light-induced swelling and bimodal photothermal/chemotherapy anticancer activity. *ACS Appl Mater Interfaces*, 2018, 10: 27631–27643
- 266 Lin H, Wang Y, Gao S, *et al.* Theranostic 2D tantalum carbide (MXene). *Adv Mater*, 2018, 30: 1703284
- 267 Yu X, Cai X, Cui H, *et al.* Fluorine-free preparation of titanium carbide MXene quantum dots with high near-infrared photothermal performances for cancer therapy. *Nanoscale*, 2017, 9: 17859–17864
- 268 Xiao F, Naficy S, Casillas G, *et al.* Edge-hydroxylated boron

- nitride nanosheets as an effective additive to improve the thermal response of hydrogels. *Adv Mater*, 2015, 27: 7196–7203
- 269 Weng Q, Wang B, Wang X, *et al.* Highly water-soluble, porous, and biocompatible boron nitrides for anticancer drug delivery. *ACS Nano*, 2014, 8: 6123–6130
- 270 Sharker SM, Alam MA, Shill MC, *et al.* Functionalized hBN as targeted photothermal chemotherapy for complete eradication of cancer cells. *Int J Pharm*, 2017, 534: 206–212
- 271 Zhang Y, Guo R, Wang D, *et al.* Pd nanoparticle-decorated hydroxy boron nitride nanosheets as a novel drug carrier for chemo-photothermal therapy. *Colloid Surface B-Biointerfaces*, 2019, 176: 300–308
- 272 Usman MS, Hussein MZ, Fakurazi S, *et al.* Gadolinium-based layered double hydroxide and graphene oxide nano-carriers for magnetic resonance imaging and drug delivery. *Chem Central J*, 2017, 11: 47
- 273 Ruan Y, Jia X, Wang C, *et al.* Mn-Fe layered double hydroxide nanosheets: A new photothermal nanocarrier for O₂-evolving phototherapy. *Chem Commun*, 2018, 54: 11729–11732
- 274 Guan S, Weng Y, Li M, *et al.* An NIR-sensitive layered supramolecular nanovehicle for combined dual-modal imaging and synergistic therapy. *Nanoscale*, 2017, 9: 10367–10374
- 275 Li B, Tang J, Chen W, *et al.* Novel theranostic nanoplatform for complete mice tumor elimination via MR imaging-guided acid-enhanced photothermo-/chemo-therapy. *Biomaterials*, 2018, 177: 40–51
- 276 Lan G, Ni K, Lin W. Nanoscale metal-organic frameworks for phototherapy of cancer. *Coord Chem Rev*, 2019, 379: 65–81
- 277 Fu G, Liu W, Feng S, *et al.* Prussian blue nanoparticles operate as a new generation of photothermal ablation agents for cancer therapy. *Chem Commun*, 2012, 48: 11567–11569
- 278 Wang D, Zhou J, Chen R, *et al.* Controllable synthesis of dual-MOFs nanostructures for pH-responsive artemisinin delivery, magnetic resonance and optical dual-model imaging-guided chemo/photothermal combinational cancer therapy. *Biomaterials*, 2016, 100: 27–40
- 279 Allison RR, Moghissi K. Photodynamic therapy (PDT): PDT mechanisms. *Clin Endosc*, 2013, 46: 24–29
- 280 Kessel D, Oleinick NL. Photodynamic therapy and cell death pathways. In: Gomer C (ed.). *Photodynamic Therapy. Methods in Molecular Biology (Methods and Protocols)*. Totowa: Humana Press, 2010, 635
- 281 Kataoka H, Nishie H, Hayashi N, *et al.* New photodynamic therapy with next-generation photosensitizers. *Ann Transl Med*, 2017, 5: 183
- 282 Kwiatkowski S, Knap B, Przysupski D, *et al.* Photodynamic therapy: Mechanisms, photosensitizers and combinations. *Biomed Pharmacother*, 2018, 106: 1098–1107
- 283 Solban N, Rizvi I, Hasan T. Targeted photodynamic therapy. *Lasers Surg Med*, 2006, 38: 522–531
- 284 Guan Q, Li YA, Li WY, *et al.* Photodynamic therapy based on nanoscale metal-organic frameworks: From material design to cancer nanotherapeutics. *Chem Asian J*, 2018, 13: 3122–3149
- 285 Lucky SS, Soo KC, Zhang Y. Nanoparticles in photodynamic therapy. *Chem Rev*, 2015, 115: 1990–2042
- 286 Wang M, Hou Z, Al Kheraif AA, *et al.* Mini review of TiO₂-based multifunctional nanocomposites for near-infrared light-responsive phototherapy. *Adv Healthc Mater*, 2018, 7: 1800351
- 287 Wu M, Li Z, Yao J, *et al.* Pea protein/gold nanocluster/indocyanine green ternary hybrid for near-infrared fluorescence/computed tomography dual-modal imaging and synergistic photodynamic/photothermal therapy. *ACS Biomater Sci Eng*, 2019, 5: 4799–4807
- 288 Yang Y, Hu Y, Du H, *et al.* Colloidal plasmonic gold nanoparticles and gold nanorings: Shape-dependent generation of singlet oxygen and their performance in enhanced photodynamic cancer therapy. *Int J Nanomed*, 2018, 13: 2065–2078
- 289 Jia X, Ye HN, Weng H, *et al.* Small molecular target-based multifunctional upconversion nanocomposites for targeted and in-depth photodynamic and chemo-anticancer therapy. *Mater Sci Eng-C*, 2019, 104: 109849
- 290 Zhao J, Duan L, Wang A, *et al.* Insight into the efficiency of oxygen introduced photodynamic therapy (PDT) and deep PDT against cancers with various assembled nanocarriers. *WIREs Nanomed Nanobiotechnol*, 2020, 12: e1583
- 291 Parekh G, Shi Y, Zheng J, *et al.* Nano-carriers for targeted delivery and biomedical imaging enhancement. *Ther Deliv*, 2018, 9: 451–468
- 292 Wei Z, Liang P, Xie J, *et al.* Carrier-free nano-integrated strategy for synergetic cancer anti-angiogenic therapy and phototherapy. *Chem Sci*, 2019, 10: 2778–2784
- 293 Ge J, Lan M, Zhou B, *et al.* A graphene quantum dot photodynamic therapy agent with high singlet oxygen generation. *Nat Commun*, 2014, 5: 4596
- 294 Zhang D, Wen L, Huang R, *et al.* Mitochondrial specific photodynamic therapy by rare-earth nanoparticles mediated near-infrared graphene quantum dots. *Biomaterials*, 2018, 153: 14–26
- 295 Dong HQ, Zhao ZL, Wen HY, *et al.* Poly(ethylene glycol) conjugated nano-graphene oxide for photodynamic therapy. *Sci China Chem*, 2010, 53: 2265–2271
- 296 Tian B, Wang C, Zhang S, *et al.* Photothermally enhanced photodynamic therapy delivered by nano-graphene oxide. *ACS Nano*, 2011, 5: 7000–7009
- 297 Patel SC, Lee S, Lalwani G, *et al.* Graphene-based platforms for cancer therapeutics. *Ther Deliv*, 2016, 7: 101–116
- 298 Youssef Z, Vanderesse R, Colombeau L, *et al.* The application of titanium dioxide, zinc oxide, fullerene, and graphene nanoparticles in photodynamic therapy. *Cancer Nano*, 2017, 8: 6
- 299 Sun X, Zebibula A, Dong X, *et al.* Aggregation-induced emission nanoparticles encapsulated with PEGylated nano graphene oxide and their applications in two-photon fluorescence bioimaging and photodynamic therapy *in vitro* and *in vivo*. *ACS Appl Mater Interfaces*, 2018, 10: 25037–25046
- 300 Zaharie-Butucel D, Potara M, Suarasan S, *et al.* Efficient combined near-infrared-triggered therapy: Phototherapy over chemotherapy in chitosan-reduced graphene oxide-IR820 dye-doxorubicin nanoplateforms. *J Colloid Interface Sci*, 2019, 552: 218–229
- 301 Tabish TA, Scotton CJ, J Ferguson DC, *et al.* Biocompatibility and toxicity of graphene quantum dots for potential application in photodynamic therapy. *Nanomedicine*, 2018, 13: 1923–1937
- 302 Liu Y, Xu Y, Geng X, *et al.* Synergistic targeting and efficient photodynamic therapy based on graphene oxide quantum dot-upconversion nanocrystal hybrid nanoparticles. *Small*, 2018, 14: 1800293
- 303 Wu C, Guan X, Xu J, *et al.* Highly efficient cascading synergy of cancer photo-immunotherapy enabled by engineered graphene quantum dots/photosensitizer/CpG oligonucleotides hybrid nanotheranostics. *Biomaterials*, 2019, 205: 106–119
- 304 Zhang D, Lin Z, Lan S, *et al.* The design of Janus black phos-

- phorus quantum dots@metal-organic nanoparticles for simultaneously enhancing environmental stability and photodynamic therapy efficiency. *Mater Chem Front*, 2019, 3: 656–663
- 305 Huang H, He L, Zhou W, *et al.* Stable black phosphorus/Bi₂O₃ heterostructures for synergistic cancer radiotherapy. *Biomaterials*, 2018, 171: 12–22
- 306 Tang X, Chen H, Ponraj JS, *et al.* Fluorination-enhanced ambient stability and electronic tolerance of black phosphorus quantum dots. *Adv Sci*, 2018, 5: 1800420
- 307 Liu J, Yu M, Zhou C, *et al.* Renal clearable inorganic nanoparticles: A new frontier of bionanotechnology. *Mater Today*, 2013, 16: 477–486
- 308 Dang J, He H, Chen D, *et al.* Manipulating tumor hypoxia toward enhanced photodynamic therapy (PDT). *Biomater Sci*, 2017, 5: 1500–1511
- 309 Lv Z, Wei H, Li Q, *et al.* Achieving efficient photodynamic therapy under both normoxia and hypoxia using cyclometalated Ru(II) photosensitizer through type I photochemical process. *Chem Sci*, 2018, 9: 502–512
- 310 Liu J, Du P, Mao H, *et al.* Dual-triggered oxygen self-supply black phosphorus nanosystem for enhanced photodynamic therapy. *Biomaterials*, 2018, 172: 83–91
- 311 Liu J, Du P, Liu T, *et al.* A black phosphorus/manganese dioxide nanoplateform: Oxygen self-supply monitoring, photodynamic therapy enhancement and feedback. *Biomaterials*, 2019, 192: 179–188
- 312 Liu B, Li C, Chen G, *et al.* Synthesis and optimization of MoS₂@Fe₃O₄-ICG/Pt(IV) nanoflowers for MR/IR/PA bioimaging and combined PTT/PDT/chemotherapy triggered by 808 nm laser. *Adv Sci*, 2017, 4: 1600540
- 313 Han J, Xia H, Wu Y, *et al.* Single-layer MoS₂ nanosheet grafted upconversion nanoparticles for near-infrared fluorescence imaging-guided deep tissue cancer phototherapy. *Nanoscale*, 2016, 8: 7861–7865
- 314 Liu L, Wang J, Tan X, *et al.* Photosensitizer loaded PEG-MoS₂-Au hybrids for CT/NIRF imaging-guided stepwise photothermal and photodynamic therapy. *J Mater Chem B*, 2017, 5: 2286–2296
- 315 Li P, Liu L, Lu Q, *et al.* Ultrasmall MoS₂ nanodots-doped biodegradable SiO₂ nanoparticles for clearable FL/CT/MSOT imaging-guided PTT/PDT combination tumor therapy. *ACS Appl Mater Interfaces*, 2019, 11: 5771–5781
- 316 Wang J, Pang X, Tan X, *et al.* A triple-synergistic strategy for combinational photo/radiotherapy and multi-modality imaging based on hyaluronic acid-hybridized polyaniline-coated WS₂ nanodots. *Nanoscale*, 2017, 9: 5551–5564
- 317 Liu G, Zou J, Tang Q, *et al.* Surface modified Ti₃C₂ MXene nanosheets for tumor targeting photothermal/photodynamic/chemo synergistic therapy. *ACS Appl Mater Interfaces*, 2017, 9: 40077–40086
- 318 Mei X, Wang W, Yan L, *et al.* Hydrotalcite monolayer toward high performance synergistic dual-modal imaging and cancer therapy. *Biomaterials*, 2018, 165: 14–24
- 319 Li X, Zheng BY, Ke MR, *et al.* A tumor-pH-responsive supramolecular photosensitizer for activatable photodynamic therapy with minimal *in vivo* skin phototoxicity. *Theranostics*, 2017, 7: 2746–2756
- 320 Yan L, Wang Y, Hu T, *et al.* Layered double hydroxide nanosheets: Towards ultrasensitive tumor microenvironment responsive synergistic therapy. *J Mater Chem B*, 2020, 8: 1445–1455
- 321 Lu K, He C, Lin W. Nanoscale metal-organic framework for highly effective photodynamic therapy of resistant head and neck cancer. *J Am Chem Soc*, 2014, 136: 16712–16715
- 322 Shi Z, Zhang K, Zada S, *et al.* Upconversion nanoparticle-induced multimode photodynamic therapy based on a metal-organic framework/titanium dioxide nanocomposite. *ACS Appl Mater Interfaces*, 2020, 12: 12600–12608
- 323 Wang D, Wu H, Lim WQ, *et al.* A mesoporous nanoenzyme derived from metal-organic frameworks with endogenous oxygen generation to alleviate tumor hypoxia for significantly enhanced photodynamic therapy. *Adv Mater*, 2019, 31: 1901893
- 324 Zeng JY, Zou MZ, Zhang M, *et al.* π -Extended benzoporphyrin-based metal-organic framework for inhibition of tumor metastasis. *ACS Nano*, 2018, 12: 4630–4640
- 325 Wang H, Chen Y, Wang H, *et al.* DNAzyme-loaded metal-organic frameworks (MOFs) for self-sufficient gene therapy. *Angew Chem Int Ed*, 2019, 58: 7380–7384
- 326 Hu X, Lu Y, Zhou L, *et al.* Post-synthesis strategy to integrate porphyrinic metal-organic frameworks with CuS NPs for synergistic enhanced photo-therapy. *J Mater Chem B*, 2020, 8: 935–944
- 327 Pan X, Wang H, Wang S, *et al.* Sonodynamic therapy (SDT): A novel strategy for cancer nanotheranostics. *Sci China Life Sci*, 2018, 61: 415–426
- 328 Pang X, Xu C, Jiang Y, *et al.* Natural products in the discovery of novel sonosensitizers. *Pharmacol Ther*, 2016, 162: 144–151
- 329 Pecha R, Gompf B. Microimplosions: Cavitation collapse and shock wave emission on a nanosecond time scale. *Phys Rev Lett*, 2000, 84: 1328–1330
- 330 Kennedy JE. High-intensity focused ultrasound in the treatment of solid tumours. *Nat Rev Cancer*, 2005, 5: 321–327
- 331 Xu J, Xu L, Wang C, *et al.* Near-infrared-triggered photodynamic therapy with multitasking upconversion nanoparticles in combination with checkpoint blockade for immunotherapy of colorectal cancer. *ACS Nano*, 2017, 11: 4463–4474
- 332 Trendowski M. The promise of sonodynamic therapy. *Cancer Metast Rev*, 2014, 33: 143–160
- 333 Liu R, Zhang Q, Lang Y, *et al.* Sonodynamic therapy, a treatment developing from photodynamic therapy. *Photodiagn Photodyn Ther*, 2017, 19: 159–166
- 334 Chen H, Zhou X, Gao Y, *et al.* Recent progress in development of new sonosensitizers for sonodynamic cancer therapy. *Drug Discov Today*, 2014, 19: 502–509
- 335 Qian X, Zheng Y, Chen Y. Micro/nanoparticle-augmented sonodynamic therapy (SDT): Breaking the depth shallow of photoactivation. *Adv Mater*, 2016, 28: 8097–8129
- 336 Xu H, Zhang X, Han R, *et al.* Nanoparticles in sonodynamic therapy: State of the art review. *RSC Adv*, 2016, 6: 50697–50705
- 337 Liu Z, Wang D, Li J, *et al.* Self-assembled peptido-nanomicelles as an engineered formulation for synergy-enhanced combinational SDT, PDT and chemotherapy to nasopharyngeal carcinoma. *Chem Commun*, 2019, 55: 10226–10229
- 338 Wang Z, Liu C, Zhao Y, *et al.* Photomagnetic nanoparticles in dual-modality imaging and photo-sonodynamic activity against bacteria. *Chem Eng J*, 2019, 356: 811–818
- 339 Karimi M, Ghasemi A, Sahandi Zangabad P, *et al.* Smart micro/nanoparticles in stimulus-responsive drug/gene delivery systems. *Chem Soc Rev*, 2016, 45: 1457–1501
- 340 Yang HW, Hua MY, Hwang TL, *et al.* Non-invasive synergistic treatment of brain tumors by targeted chemotherapeutic delivery

- and amplified focused ultrasound-hyperthermia using magnetic nanographene oxide. *Adv Mater*, 2013, 25: 3605–3611
- 341 Chen YW, Liu TY, Chang PH, *et al.* A theranostic nrGO@MSN-ION nanocarrier developed to enhance the combination effect of sonodynamic therapy and ultrasound hyperthermia for treating tumor. *Nanoscale*, 2016, 8: 12648–12657
- 342 Dai C, Zhang S, Liu Z, *et al.* Two-dimensional graphene augments nanosensitized sonocatalytic tumor eradication. *ACS Nano*, 2017, 11: 9467–9480
- 343 Fang C, Jia H, Chang S, *et al.* (Gold core)/(titania shell) nanostructures for plasmon-enhanced photon harvesting and generation of reactive oxygen species. *Energy Environ Sci*, 2014, 7: 3431–3438
- 344 Ma L, Huang Y, Hou M, *et al.* Ag nanorods coated with ultrathin TiO₂ shells as stable and recyclable sens substrates. *Sci Rep*, 2015, 5: 15442
- 345 Deepagan VG, You DG, Um W, *et al.* Long-circulating Au-TiO₂ nanocomposite as a sonosensitizer for ROS-mediated eradication of cancer. *Nano Lett*, 2016, 16: 6257–6264
- 346 Gao F, He G, Yin H, *et al.* Titania-coated 2D gold nanoplates as nanoagents for synergistic photothermal/sonodynamic therapy in the second near-infrared window. *Nanoscale*, 2019, 11: 2374–2384
- 347 Chen J, Qiu F, Xu W, *et al.* Recent progress in enhancing photocatalytic efficiency of TiO₂-based materials. *Appl Catal A-Gen*, 2015, 495: 131–140
- 348 Ratanatawanate C, Chyao A, Balkus Jr. KJ. S-nitrosocysteine-decorated PbS QDs/TiO₂ nanotubes for enhanced production of singlet oxygen. *J Am Chem Soc*, 2011, 133: 3492–3497
- 349 Chen L, Zhang C, Li L, *et al.* Ultrafast carrier dynamics and efficient triplet generation in black phosphorus quantum dots. *J Phys Chem C*, 2017, 121: 12972–12978
- 350 Ouyang J, Deng L, Chen W, *et al.* Two dimensional semiconductors for ultrasound-mediated cancer therapy: The case of black phosphorus nanosheets. *Chem Commun*, 2018, 54: 2874–2877
- 351 Guo T, Wu Y, Lin Y, *et al.* Black phosphorus quantum dots with renal clearance property for efficient photodynamic therapy. *Small*, 2018, 14: 1702815
- 352 Guo Z, Chen S, Wang Z, *et al.* Metal-ion-modified black phosphorus with enhanced stability and transistor performance. *Adv Mater*, 2017, 29: 1703811
- 353 Zhao Y, Wang H, Huang H, *et al.* Surface coordination of black phosphorus for robust air and water stability. *Angew Chem Int Ed*, 2016, 55: 5003–5007
- 354 Hu T, Mei X, Wang Y, *et al.* Two-dimensional nanomaterials: Fascinating materials in biomedical field. *Sci Bull*, 2019, 64: 1707–1727
- 355 Lyu Q, Zhang J, Neoh KG, *et al.* A one step method for the functional and property modification of DOPA based nanocoatings. *Nanoscale*, 2017, 9: 12409–12415
- 356 Zhou W, Cui H, Ying L, *et al.* Enhanced cytosolic delivery and release of CRISPR/Cas9 by black phosphorus nanosheets for genome editing. *Angew Chem Int Ed*, 2018, 57: 10268–10272
- 357 Krug HF, Wick P. Nanotoxicology: An interdisciplinary challenge. *Angew Chem Int Ed*, 2011, 50: 1260–1278
- 358 Peng F, Setyawati MI, Tee JK, *et al.* Nanoparticles promote *in vivo* breast cancer cell intravasation and extravasation by inducing endothelial leakiness. *Nat Nanotechnol*, 2019, 14: 279–286
- 359 Martins AF, Follmann HDM, Monteiro JP, *et al.* Polyelectrolyte complex containing silver nanoparticles with antitumor property on Caco-2 colon cancer cells. *Int J Biol Macromol*, 2015, 79: 748–755
- 360 Rao PV, Nallappan D, Madhavi K, *et al.* Phytochemicals and biogenic metallic nanoparticles as anticancer agents. *Oxid Med Cell Longev*, 2016, 2016: 1–15

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Conflict of interest The authors declare that they have no conflict of interest.

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近红外或超声敏感的二维纳米材料用于癌症诊疗的研究进展

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摘要 二维纳米材料在电子学、催化、超级电容器和能源材料等领域展现出了巨大的应用潜力。在生物医学领域,以二维超薄纳米材料为代表的低维材料,因其优异的机械、光热、电子和光学性能,以及良好的生物相容性和生物降解性,被广泛用于构建多功能纳米平台并应用于肿瘤的诊疗。本综述概述了石墨炔、黑磷、过渡金属二卤化物、锑烯等新型低维材料的特定结构与性质,详细总结了基于各类对近红外或超声敏感的材料构建的纳米平台在光热、光动力和声动力无创肿瘤治疗中的最新进展,并进一步探讨了纳米材料在无创式癌症治疗中所面临的挑战与应用前景。