

The Advancing Role of Nanocomposites in Cancer Diagnosis and Treatment

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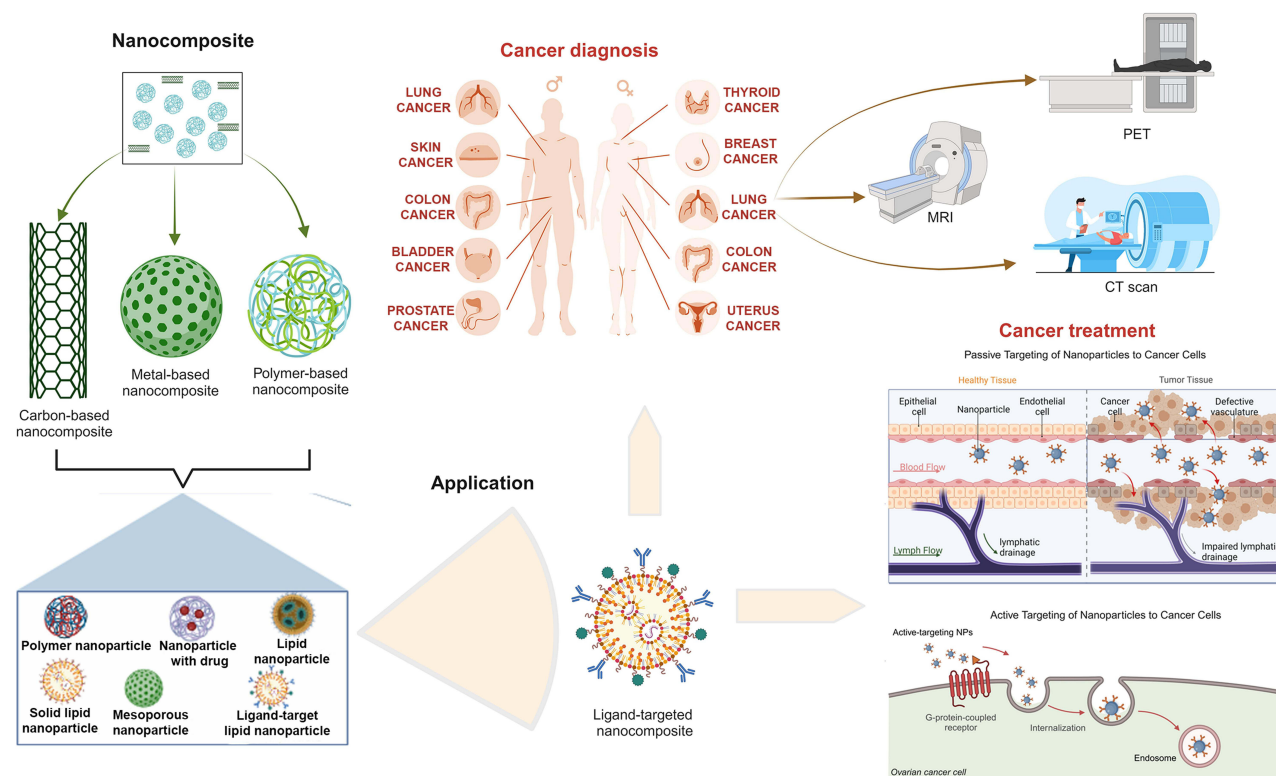
Abstract: The relentless pursuit of effective cancer diagnosis and treatment strategies has led to the rapidly expanding field of nanotechnology, with a specific focus on nanocomposites. Nanocomposites, a combination of nanomaterials with diverse properties, have emerged as versatile tools in oncology, offering multifunctional platforms for targeted delivery, imaging, and therapeutic interventions. Nanocomposites exhibit great potential for early detection and accurate imaging in cancer diagnosis. Integrating various imaging modalities, such as magnetic resonance imaging (MRI), computed tomography (CT), and fluorescence imaging, into nanocomposites enables the development of contrast agents with enhanced sensitivity and specificity. Moreover, functionalizing nanocomposites with targeting ligands ensures selective accumulation in tumor tissues, facilitating precise imaging and diagnostic accuracy. On the therapeutic front, nanocomposites have revolutionized cancer treatment by overcoming traditional challenges associated with drug delivery. The controlled release of therapeutic agents from nanocomposite carriers enhances drug bioavailability, reduces systemic toxicity, and improves overall treatment efficacy. Additionally, the integration of stimuli-responsive components within nanocomposites enables site-specific drug release triggered by the unique microenvironment of the tumor. Despite the remarkable progress in the field, challenges such as biocompatibility, scalability, and long-term safety profiles remain. This article provides a comprehensive overview of recent developments, challenges, and prospects, emphasizing the transformative potential of nanocomposites in revolutionizing the landscape of cancer diagnostics and therapeutics. In Conclusion, integrating nanocomposites in cancer diagnosis and treatment heralds a new era for precision medicine.

Keywords: nanocomposites, cancer, diagnosis, therapy, nanoparticles, theranostic

Introduction

Nanocomposites belong to a broader class of intentionally produced materials called nanomaterials, which incorporate nanosized particles into a matrix of standard materials. These nanosized particles can have one, two, or three dimensions of less than 100 nanometers.¹ Integrating nanoscale components imparts unique characteristics to the composite material, making nanocomposites valuable in various applications, including healthcare.² The tunable properties of nanocomposites, such as biocompatibility, stimuli responsiveness, and functionality, have deemed them ideal platforms for diagnosing and treating chronic diseases, including cancer, diabetes, and cardiovascular disease.^{2,3} In the phase of increasing cancer cases and deaths, there is a growing global cancer burden and a need for effective theranostic strategies. Researchers aim to speed up cancer diagnosis with efforts to reduce waiting times and enhance the efficiency of the diagnostic process for patients.⁴ Nanocomposites have emerged as unique particles, promising to revolutionize cancer diagnosis and treatment.

Graphical Abstract



In their specific application in cancer, nanocomposites play a crucial role in advancing cancer diagnosis and treatment as they are employed in various applications for precise and effective strategies in the fight against cancer.⁵ While nanomaterials contribute to precise applications for cancer detection and diagnosis, aiming to synthesize nanomaterials for improved efficacy,⁶ nanotechnology, which encompasses applications like drug delivery, has yielded promising results in cancer diagnosis and treatment and continues to contribute to advancements in the field.⁷ For instance, the application of molybdenum disulfide (MoS_2)-based nanocomposites, including its biosensors, bioimaging, photoredox catalysis, and antibacterial properties, show promise in cancer diagnosis and therapy and contribute to the development of innovative approaches.^{5,7} Various nanocomposites, such as gold nanorods loaded, chitosan conjugated, and pluronic-based nanocarriers, serve as imaging agents for cancer cells and hyperthermic agents, showcasing their versatility in cancer diagnosis and treatment.⁸ Moreover, bio-nanotechnology, a subset of nanotechnology, is applied in tumor diagnosis and treatment, providing effective support through targeting and gene therapy.^{8,9} For example, nanocomposites of graphene oxide-silver nanoparticles and cisplatin strongly potentiate cisplatin-induced cytotoxicity, apoptosis, and autophagy in human cancer cells.¹⁰ A bio-graphene-based multifunctional nanocomposites also exhibited intracellular drug delivery in cervical cancer treatment.⁹

In diagnostics, nanocomposites serve as both imaging agents and biosensors. Metal-based nanomaterials and nanocomposites are utilized as contrast agents in cancer imaging, gaining attention for their unique properties in diagnostics.¹¹ Bio-nanotechnology-based cell biosensors also exhibit high sensitivity and speed in detecting and distinguishing different types of tumor cells, contributing to tumor diagnosis.⁸ Nanoparticles serve as effective drug carriers for diseases like cancer due to their small size and increased stability, enhancing targeted drug delivery partly via encapsulating active pharmaceutical ingredients.¹² Considering the growing interest and rapid data expansion in this field, we review the progress made in recent years. The synthesis and characterization of nanocomposites and their application in cancer diagnosis and treatment are explored. The advances made, challenges, and prospects are also discussed.

Synthesis and Characterization of Nanocomposites for Cancer Applications

The synthesis and characterization of nanocomposites for cancer applications involve a series of crucial steps determining their efficacy and safety. The synthesis typically involves the combination of nanoparticles with various polymers or other materials to form a composite structure. Various techniques can be employed for synthesis, including the sol-gel method, in-situ polymerization, and layer-by-layer (LbL) assembly.^{13,14} While the sol-gel method involves the hydrolysis and condensation of precursors to form a gel network that encapsulates nanoparticles, the in-situ polymerization involves the polymerization of monomers in the presence of nanoparticles, leading to their incorporation into the polymer matrix. The LbL assembly involves a sequential deposition of oppositely charged nanoparticles and polymers to form a multilayer structure.^{13–15} Characterization techniques play a pivotal role in evaluating the properties and performance of nanocomposites for cancer applications. Common characterization techniques include dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), and Fourier transform infrared spectroscopy (FTIR)^{14–17} (Figure 1). Each of these techniques provides a unique assessment of the properties of the nanocomposite. DLS measures the particle size distribution of nanoparticles in the nanocomposite, SEM provides high-resolution images of the surface morphology and structure, TEM offers detailed information about the internal structure and morphology, and XRD determines the crystal structure and crystallinity of the nanocomposite. Moreover, FTIR is used to identify the functional groups in the nanocomposite.^{16,18} Researchers can design nanocomposites with optimized properties for cancer diagnosis, therapy, and theranostics by carefully tailoring the synthesis and

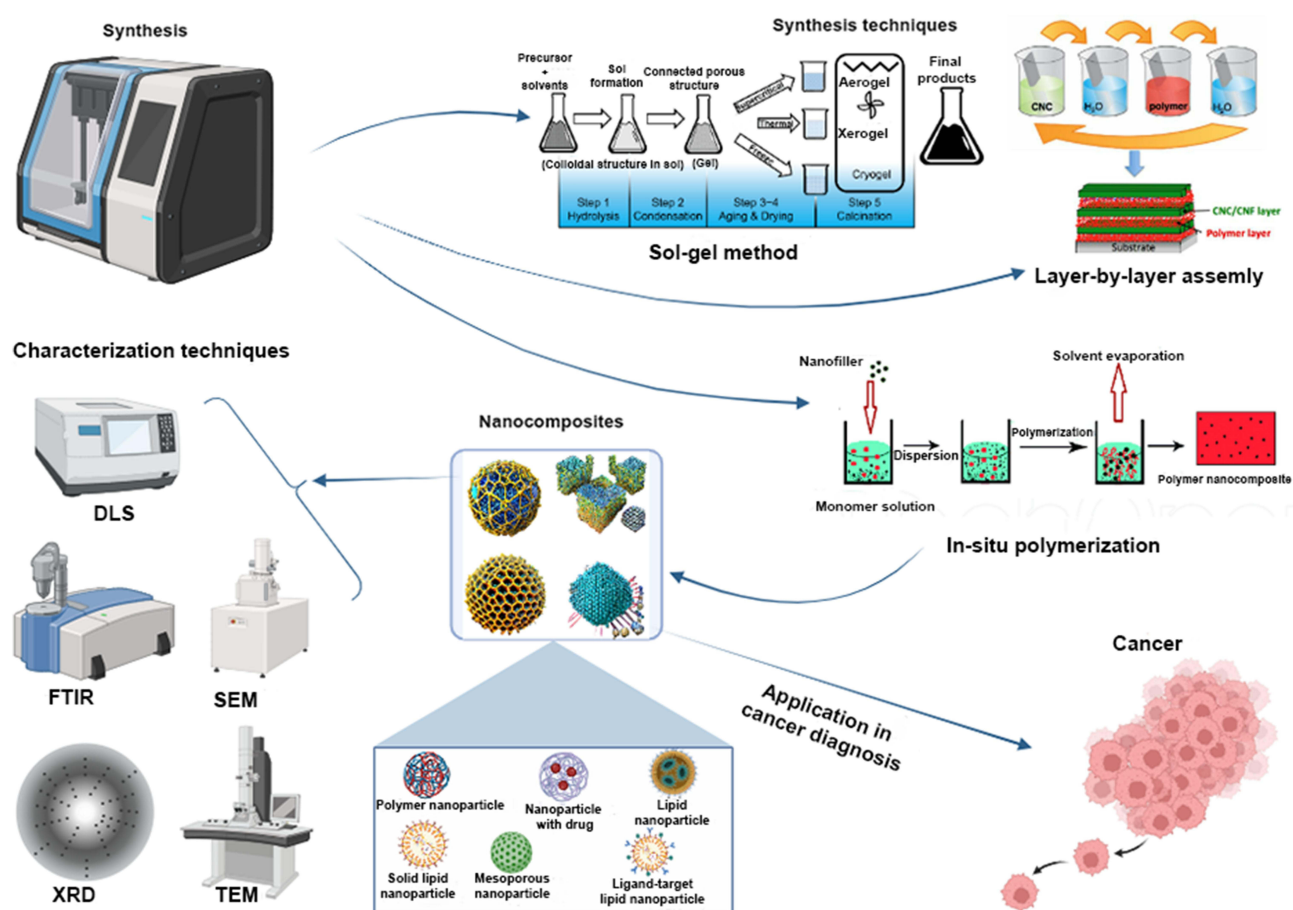


Figure 1 Synthetic and characterization techniques. Nanocomposites are synthesized using the sol-gel method, in-situ polymerization, and layer-by-layer (LbL) assembly. This is followed by evaluating the properties and performance of nanocomposites through techniques that include.

Abbreviations: DLS, dynamic light scattering; SEM, scanning electron microscopy; TEM, transmission electron microscopy; XRD, X-ray diffraction; FTIR, Fourier transform infrared spectroscopy.

characterization processes. These nanocomposites offer promising advancements in cancer treatment by enhancing drug delivery, targeting tumor cells, and improving therapeutic efficacy while minimizing side effects.

The synthesis and characterization of nanocomposites for cancer applications also involve developing advanced materials with unique properties tailored for diagnosis and treatment. Recent research highlights notable examples include smart supermagnetic nanocomposites,¹⁴ Yttrium oxide nanocomposites,¹⁹ ZnO–TiO₂–Chitosan–Escin nanocomposites,¹⁵ branched magnetic nanocomposites,¹⁸ and Copper Oxide–Titanium Oxide–Chitosan–Amygdalin nanocomposites.¹⁷ Supermagnetic nanocomposites, based on iron oxide nanoparticles coated with Pluronic F127, have been synthesized for targeted drug delivery in cancer therapy,¹⁴ and polymer-gated and superparamagnetic nanoparticle embedded hollow mesoporous silica nanoparticles as a smart multifunctional nanocarrier for targeted and controlled drug delivery for cancer treatment.²⁰ These studies emphasize nanocomposites' smart design for potential cancer treatment applications. Other nanocomposites have been synthesized to carry bio-macromolecules and therapeutic agents,^{18,20} implicating the potential of these nanocomposites for cancer diagnostic and therapeutic applications.

Regardless of the progress made in this field, the synthesis and characterization of nanocomposites present several key challenges and considerations that must be addressed to ensure the successful development of these materials with desired properties. These challenges are broadly categorized into synthesis challenges (including uniform dispersion of nanoparticles, surface interactions, and scalability of synthesis methods)^{21–23} and characterization challenges (including accuracy in characterizing the size, shape, and distribution, interfacial characterization, and property evaluation).^{21,22,24} Addressing these challenges and considerations is crucial for advancing nanocomposite technology and developing materials with tailored properties for a wide range of applications.

Nanocomposites in Cancer Diagnosis

Nanocomposites have emerged as promising materials for cancer diagnosis due to their unique properties that can enhance sensitivity, specificity, and imaging resolution.^{25,26} These materials are composed of two or more phases at the nanoscale, with one phase typically being a nanoparticle and the other being a polymer or other matrix material. The nanoparticles can be tailored to interact with specific cancer biomarkers, while the matrix material provides stability and biocompatibility.^{7,27} The use of nanocomposites in cancer diagnosis offers several advantages over traditional diagnostic methods. Nanocomposites exhibit enhanced sensitivity as they can detect smaller amounts of cancer cells or biomarkers, leading to earlier detection of cancer⁷ and improved specificity as they can be targeted to specific cancer cells, reducing the risk of false positives.²⁶ More importantly, nanocomposites possess multifunctional capabilities and combine diagnostic and therapeutic functions, enabling theranostic approaches.⁷ Several types of nanocomposites have been investigated for cancer diagnosis, including metal-, carbon-, and polymer-based nanocomposites.

Gold, silver, and iron oxide nanoparticles are commonly used metal-based nanoparticles in cancer diagnostics. These nanoparticles can be conjugated to antibodies or other targeting ligands to specifically bind to cancer cells. They serve as contrast agents and can be detected using various imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET)^{25,26} (Figure 2). Interestingly, metal-based nanoparticles induce antitumor immune responses, contributing to their potential in cancer diagnostics by leveraging cellular and molecular mechanisms.^{28,29} Carbon nanotubes, graphene oxide, and fullerene derivatives have also been explored for cancer diagnosis as carbon-based nanomaterials. These nanomaterials have unique optical properties that can be used for fluorescence or photoacoustic imaging. They can also be used to deliver diagnostic agents or drugs to cancer cells.^{25,26} Polymeric nanocomposites can be designed with controlled size, shape, and surface properties, making them suitable for various diagnostic applications. They can encapsulate diagnostic agents, such as fluorescent dyes or radioactive isotopes, and release them in a controlled manner at the tumor site.⁷ Despite the promising potential of these nanocomposites in cancer diagnosis, further research is needed to address challenges such as biocompatibility, long-term safety, and scalable production.

Properties and Mechanisms of Nanocomposites in Cancer Diagnosis

High Surface Area

Nanoparticles have a large surface area-to-volume ratio, allowing them to interact with many molecules. This makes them ideal for carrying and delivering diagnostic agents. The high surface area, which arises from the presence of nanoscale

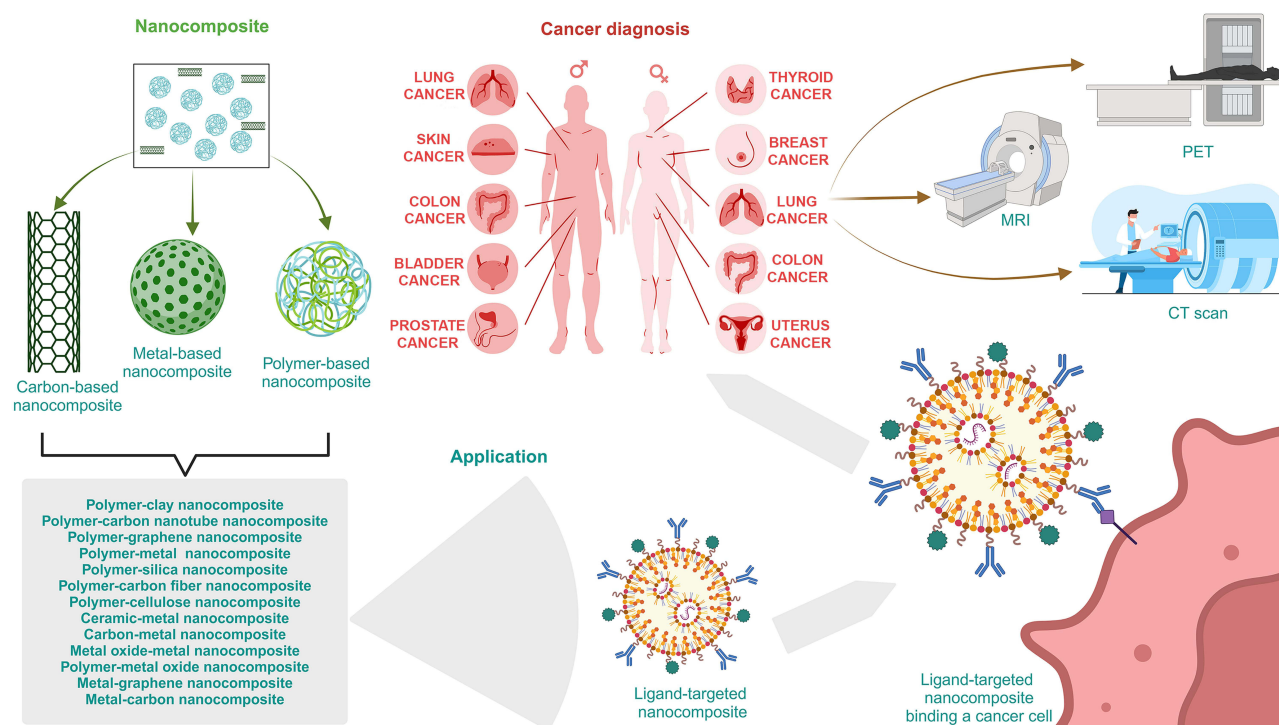


Figure 2 Types of nanocomposites in cancer diagnosis. The nanocomposites used in cancer diagnosis include metal-, carbon-, and polymer-based nanocomposites. In a typical application, a ligand-targeted nanocomposite designed to bind cancer cells explicitly targets tumors in the host. The resultant complex serves as a contrast agent that can be detected using various imaging techniques such as.

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

features, contributes to various enhanced properties and functionalities in nanocomposite materials, including increased strength and stiffness, enhanced thermal conductivity, improved electrical conductivity, enhanced gas barrier properties, increased catalytic activity, and improved drug delivery systems.^{30,31} For example, in polymer-based nanocomposites such as carbon nanotube-polymer nanocomposites, the addition of nanoscale reinforcements like clay nanoparticles can significantly increase the strength and stiffness of the composite material. The high surface area of the nanoparticles allows for a more efficient load transfer within the matrix, leading to improved mechanical properties.³² Carbon nanotubes are known for their excellent thermal conductivity. When incorporated into a polymer matrix, the high surface area of individual nanotubes facilitates efficient heat transfer between them, resulting in a nanocomposite with enhanced thermal conductivity compared to the pure polymer.^{32,33} In addition, titanium dioxide (TiO₂) nanocomposites: TiO₂, a widely used photocatalyst, can be incorporated into nanocomposites to enhance their photocatalytic activity.³⁴ TiO₂³⁴ and zeolite-polymer nanocomposites (porous, crystalline aluminosilicates)³⁵ have large surface areas, which provide more active sites for photocatalysis and improved separation and catalytic properties, respectively. These advancements make nanocomposites promising materials for various applications in healthcare, including cancer diagnosis.

Biocompatibility

Nanocomposites can be designed to be biocompatible, ensuring their safe use in the body. This is important for cancer diagnosis, as diagnostic agents need to be able to reach tumors without causing harm to healthy tissues. Several factors influence the Biocompatibility of nanocomposites, including the type of nanofiller, its size, shape, surface chemistry, and the distribution of the nanofiller within the matrix.^{28,29} Current data shows that biodegradable and biocompatible polymer nanocomposites are gaining traction in biomedical applications and are often used in diagnostic and drug delivery systems, showing compatibility with biological systems and reducing the risk of adverse reactions.³⁶ Metal oxide nanocomposites, such as zinc oxide (ZnO) and titanium dioxide (TiO₂),³⁷ and carbon-based nanocomposites, such as carbon nanotubes and graphene,³⁸ have been shown to be biocompatible and can be used in biosensors for detecting various analytes, including glucose, DNA, and proteins. Degradable nanocomposites are particularly appealing for

diagnostic applications as the body can break them down after fulfilling their diagnostic purpose, minimizing the risk of long-term accumulation.³⁹ In immunological applications, nanomaterials revolutionize medicine by enabling novel sensing, diagnostic, and therapeutic approaches. Their biocompatibility is crucial in applications that involve interaction with the immune system for targeted diagnostics or drug delivery.²⁸ The biocompatibility of nanocomposites is an ongoing area of research, and new materials with improved biocompatibility are being developed. As our understanding of the factors that influence biocompatibility deepens, nanocomposites are poised to play an increasingly important role in various diagnostic applications, including cancer.

Targeted Delivery

Nanocomposites play a crucial role in cancer diagnosis through targeted delivery systems, offering enhanced precision and effectiveness of cancer detection, leading to earlier diagnosis and improved treatment outcomes. Nanoparticles can be conjugated to antibodies or other targeting ligands to specifically bind to cancer cells.⁴⁰ This allows for the accumulation of diagnostic agents at the tumor site, improving sensitivity and reducing off-target effects. For instance, MoS₂-based nanocomposites are employed for cancer diagnosis and imaging. These nanomaterials, integrated with targeting ligands, enable selective binding to cancer cells, improving the accuracy of diagnostic imaging.⁷ Additionally, magnetic nanoparticles can be manipulated using external magnetic fields, allowing for targeted delivery to specific regions of the body. Once internalized within tumor cells, nanocomposites can release diagnostic agents, such as fluorescent dyes or molecular probes, which can specifically bind to or interact with tumor-associated biomarkers.^{41,42} The emitted fluorescence or molecular signals can then be detected using various imaging techniques, such as fluorescence microscopy or bioluminescence imaging, providing precise information about the location and extent of tumor growth.⁴³ With ongoing efforts to optimize design and characterization for specific diagnostic applications, this active area of research offers great promise for cancer diagnosis.

Enhanced and Targeted Imaging

Mechanisms contributing to enhanced and targeted imaging include enhanced permeability and retention effect, active targeting, and targeted delivery. Nanoparticles with small sizes can exploit the leaky vasculature of tumors, allowing them to extravasate into the tumor tissue and accumulate there.⁴⁴ Nanocomposites in targeted imaging can incorporate various imaging agents, such as fluorescent dyes, radioisotopes, or magnetic nanoparticles, which can be used to visualize tumors using different imaging techniques, such as fluorescence imaging, positron emission tomography (PET) or magnetic resonance imaging (MRI). Moreover, Nanoparticles conjugated to antibodies can be used to target and image cancer cells using CT or MRI.⁴⁵ Nanocomposites facilitate deeper tissue penetration and improved imaging capabilities, aiding in the precise diagnosis of cancer. The distinctive optical, magnetic, and chemical characteristics of nanoscale materials enable the development of imaging probes featuring enhanced contrast, heightened sensitivity, regulated biodistribution, improved spatial and temporal details, versatile functionality, and the ability to engage in multimodal imaging, spanning MRI, PET, SPECT, and ultrasound.^{25,46} This maturity of this property of nanocomposites holds the potential to lead to earlier and more accurate detection of tumors.

Bioresponsive Imaging

Nanocomposites can be designed to respond to specific changes in the tumor environment, such as pH, temperature, or hypoxia, and release imaging agents in response to these changes.⁴⁷ Studies report the synthesis of a protease-triggered bioresponsive drug delivery platform for the targeted theranostics of malignancy. The exceptional ability of proteases for biological recognition and catalysis, along with the impressive physicochemical properties of nanomaterials, leads to the development of nano-drug delivery systems (nanoDDS) activated by enzymes. These systems exhibit theranostic functions, responding highly specifically to stimuli associated with the tumor phenotype.⁴⁸ Similarly, a nanogel multi-enzyme mimics synthesized by biocatalytic atomic transfer radical polymerization (ATRP) and metal coordination for bioresponsive fluorescence imaging has been reported. Studies involving both cells and tumor-bearing mice confirm the achievement of effective biofluorescence imaging responsive to reactive oxygen species (ROS) using multienzyme-mimic nanogels (MPGs).⁴⁹ These observations indicate that bioresponsive nanocomposites respond to specific biological cues in the tumor environment, altering their properties and enhancing their imaging capabilities, and hold great promise for cancer diagnosis.

Electrochemical Sensing

Nanocomposites can be used to create electrochemical biosensors that can detect cancer biomarkers in the blood or other bodily fluids.⁵⁰ Graphene, a versatile nanomaterial, is employed in electrochemical biosensors for cancer diagnosis. These sensors demonstrate the potential for rapid, sensitive, and cost-effective detection of cancer biomarkers. For instance, graphene-assisted sensors have been explored for the detection of pancreatic cancer biomolecules such as the K-Ras gene, CEA, and microRNA.⁵¹ Nanocomposite applications have also been documented for the sensitive electrochemical detection of a broad range of cancer biomarkers, including circulating tumor cells, proteins, DNA mutations, and non-coding RNAs like miRNA, glycoproteins, and metabolites.⁵² Recent developments in electrochemical biosensors also utilize polymer nanocomposites (PNCs) containing metallic nanoparticles and carbon nanomaterials to enhance the sensor's performance, improving diagnostic sensitivity and selectivity.⁵³ Additionally, electrochemical sensing platforms offer label-free detection,⁵⁴ providing a versatile and efficient means to detect cancer-related molecules.

Magnetic Separation

Magnetic separation of nanocomposites relies on the principle that magnetic nanoparticles (MNPs) can be manipulated using external magnetic fields. When exposed to a magnetic field, MNPs align with the field lines, allowing for their selective separation from other particles. In the context of cancer diagnosis, MNPs can be conjugated with biomolecules that specifically bind to tumor cells or biomarkers. Upon exposure to a magnetic field, these MNPs will accumulate at the site of the tumor, facilitating their isolation and characterization.^{55,56} Magnetic nanoparticles are widely employed in cancer diagnosis for tumor imaging. MRI utilizes the magnetic properties of nanoparticles to provide detailed and high-contrast images of tumors.⁵⁶ Hybrid magnetic nanostructures are also applied in magnetic separation, diagnostics, and cancer drug delivery. These multifunctional nanocomposites enable magnetic separation to isolate cancer cells from complex biological samples efficiently, facilitating downstream analysis and diagnosis.⁵⁷ Moreover, magnetic nanoparticles can be used to capture and isolate circulating tumor cells (CTCs) from the blood. For example, ferroplatinum iron oxide ($\text{Fe}_3\text{O}_4\text{-FePt}$) magnetic nanocomposites can capture and separate CTCs.⁵⁸ This technology holds significance in cancer diagnosis and prognosis, allowing for the isolation and analysis of CTCs from blood samples. Magnetic separation offers the potential for multimodal imaging as the nanoparticles can be loaded with imaging agents, enabling simultaneous diagnosis and imaging and providing a more comprehensive understanding of the tumor. It also assists in isolating and detecting tumor-associated biomarkers, such as proteins, DNA, or RNA, for early cancer detection and prognosis.^{55,56,59} The features of nanocomposites and techniques in cancer diagnosis are illustrated in Figure 3.

Key Nanocomposites-Based Cancer Diagnostic Techniques

Application of Imaging Techniques

Nanocomposites can be used to enhance the contrast and sensitivity of imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET). For instance, iron oxide nanoparticles can be used as MRI contrast agents to improve the visualization of tumors.²⁵ The co-application of ferumoxytol, an iron oxide nanoparticle, and gadolinium-contrasted MRI helps identify pseudoprogression in glioblastoma.⁶⁰ Thus, ultrasmall superparamagnetic iron oxide nanoparticles are an emerging tool in MRI diagnostics of tumors and can add clinically useful information due to their distinct physicochemical features and biodistribution, while having a good safety profile.⁶¹ Magnetic nanoparticles conjugated with the radiotracer ^{67}Ga -DOTATATE have been used for PET imaging of neuroendocrine tumors. These nanoparticles exhibit enhanced accumulation in tumor tissues and provide accurate tumor localization.⁶² A multimodal cancer-targeted imaging system capable of concurrent fluorescence imaging, radionuclide imaging, and MRI in vivo has been reported. The researchers demonstrated that the nanocomposite, MFR-AS1411, exhibits specific fluorescence signals and specifically targets cancer cells, providing a potential versatile imaging tool for specific cancer diagnosis.⁶³ Similarly, a nanocomposite made up of poly(catechin) capped-gold nanoparticles (Au@PC NPs) and smaller nucleolin-binding aptamer (AS1411) conjugated gold NPs (AS1411-Au NPs), served as a targeting agent in LDI-MS (laser desorption/ionization mass spectrometry)-based tumor tissue imaging. The satellite-like AS1411-Au NPs/ Au@PC NP nanocomposite showed enhanced multivalent binding with nucleolin molecules on tumor cell membranes and ultrahigh signal amplification, improving LDI-MS

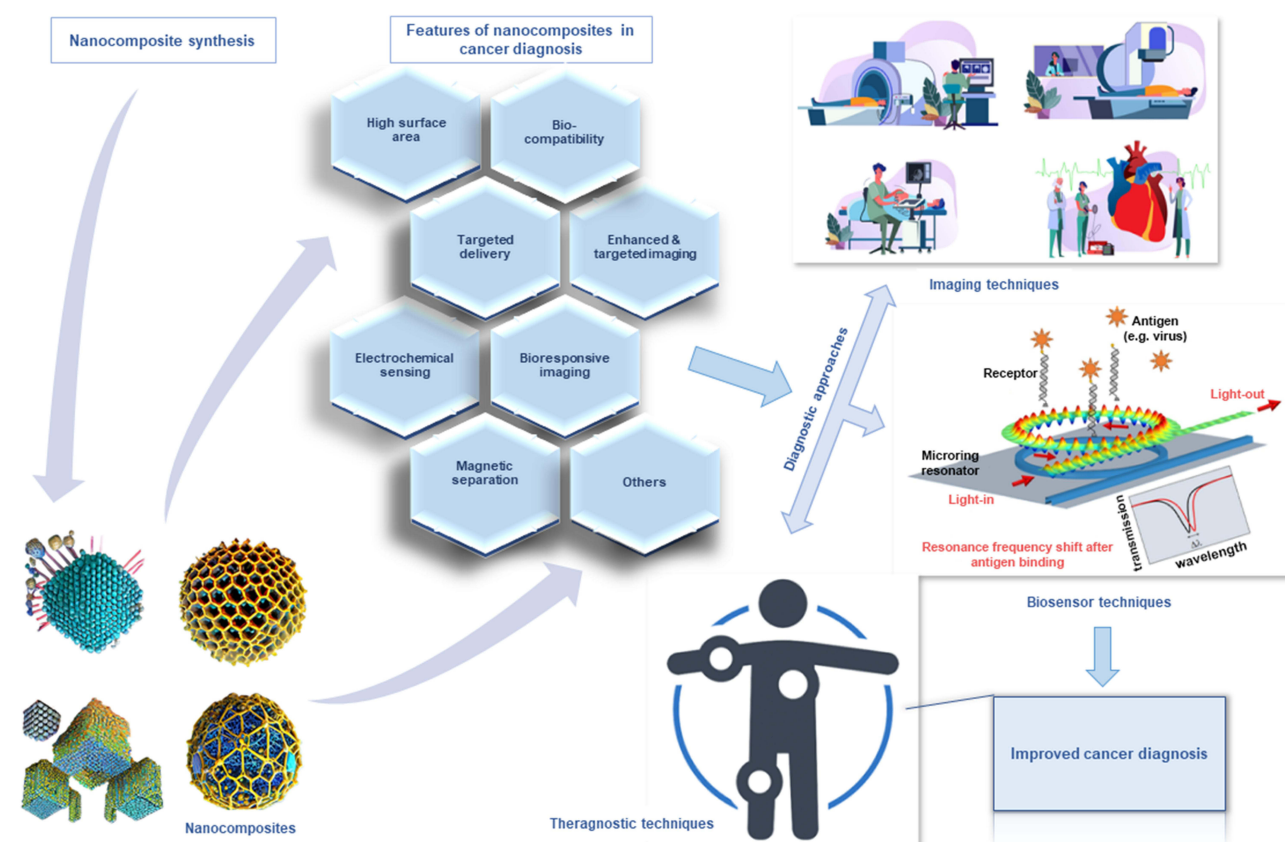


Figure 3 Features of nanocomposites and techniques in cancer diagnosis. Several properties enhance the function and diagnostic performance of nanocomposites. These properties improve cancer imaging and biosensing in diagnostics and theranostics.

imaging.⁶⁴ It is also reported that a nanocomposite consisting of magnetic PPy/Fe₃O₄-core and a gold nanoshell effectively enhances the contrast for both MRI and X-ray CT imaging in identifying cancer cells. It also provides an effective platform for multimodal imaging-guided cancer treatment.⁶⁵

Optical imaging techniques, such as photoacoustic tomography (PAT) and fluorescence imaging, are also being explored for cancer diagnosis using nanocomposites.⁶⁶ Photoacoustic and CT imaging have also been applied in tumor theranostics using a core-shell Au@Cu₂-xSe heterogeneous metal nanocomposite.⁶⁷ Fluorescent nanoparticles, such as quantum dots or upconversion nanoparticles, can emit light upon excitation, allowing for visualization of tumors. Nanocomposites can incorporate these fluorescent nanoparticles into their structure, enhancing their stability and targeting capabilities. For example, gold nanoparticles conjugated with fluorescent dyes have been used for fluorescence imaging of breast cancer cells.⁶⁸ Other studies report precision delivery of theranostic agents via thermosensitive polymer dot nanocomposites for trimodal CT/photoacoustic/fluorescence imaging in tumors.⁶⁹ In all, optical imaging offers a high potential for noninvasive detection of cancer in humans, where unspecific contrast agents such as indocyanine green (ICG) and omocyanine have been applied, whereas molecular probes for direct targeted imaging of tumors are still in preclinical research.⁷⁰ Additionally, the safety of CD8 PET imaging using ⁸⁹Zr-Df-IAB22M2C is confirmed in clinical studies, demonstrating the capability to observe the distribution of CD8+ immune cells throughout the entire body in both tumors and normal tissues.⁷¹ Additionally, it holds promise in tumor diagnostics and predicting early responses to immunotherapy.

Biosensor Application

Nanocomposites can be incorporated into biosensors to detect cancer biomarkers in biological fluids or tissues, such as proteins, nucleic acids, and metabolites. These biosensors can provide rapid, sensitive, and specific detection of cancer.⁴⁵ Label-free biosensors based on nanostructure are believed to be superior to the traditional methods in detection speed, sensitivity, cost, and versatility.³³ Biosensors in cancer diagnosis can be grouped into broader application scopes such as

electrochemical biosensors, field effect transistor (FET) biosensors, and fluorescent biosensors. Electrochemical biosensors detect biomarkers by converting their interaction with bioreceptors into measurable electrical signals. For example, MoS₂-based electrochemical sensors have successfully detected tumor markers like H₂O₂, carcinoembryonic antigen (CEA), circulating tumor cells (CTCs), and miRNA.⁷² A study reports that AuPtPd/rGO-modified GCE (glassy carbon electrode) nanocomposites serve as an excellent biosensor for monitoring the release of H₂O₂ from living cancer cells,⁷³ providing a foundation for biological and biomedical applications such as early cancer diagnosis. A 3D nanocomposite that not only exhibits a large surface area and favorable microenvironment but also possesses remarkable stability, conductivity, and biocompatibility was employed as a biosensor for CEA detection. The AuNPs/PB-PEDOT modified immunosensor could detect a CEA range of 0.05–40 ng mL⁻¹, with a detection limit of 0.01 ng mL⁻¹.⁷⁴ Since CEA, as a clinical tumor marker, can be expressed in lung, breast, ovarian, cystadenocarcinoma, and other cancers, monitoring its levels could help detect, diagnose, and manage these cancers.⁷⁵ In other cancers, such as prostate cancer, detecting sarcosine content in blood or urine has been considered to provide a basis for the diagnosis. In exploring this concept, Ti₃ C2 TX /Pt-Pd nanocomposite with excellent electrochemical performance and high stability was applied on a GCE with sarcosine oxidase (Sox) to form a sarcosine biosensor (GCE/Ti₃ C2 TX /Pt-Pd/SOx). The biosensor, capable of detecting sarcosine concentration of 1–1000 μM with a low limit of detection of 0.16 μM and a sensitivity of 84.1 μA/mM cm², exhibits potential in the early diagnosis of prostate cancer.⁷⁶ Similar nanocomposite-based biosensor platforms that detect sarcosine in prostate cancer have been reported.^{77,78}

Moreover, the combined utilization of a PEG polymer film and Au nanoparticle mixed interface enables high levels of sensitivity and effective assaying of the breast cancer susceptibility gene (BRCA1) in patient samples. The label-free DNA sensor shows feasible clinical application for breast cancer diagnosis via the BRCA1 gene.⁷⁹ Similarly, a polymer nanocomposite-modified GCE poly (dopamine beta cyclodextrine-cetyl trimethylammonium bromide) fixed with silver NPs (P[DA-β-CD /CTAB])-AgNPs-GCE) was synthesized for BRCA1 biomarkers detection. The researchers observed satisfactory biosensor results in detecting BRCA1 in human plasma samples and MCF-7 cancer cell lysates,⁸⁰ implicating the potential of the immunoassay to be applied in clinical analysis. Polymers can also be combined with nanomaterials to create biosensors with tailored properties for detecting a wide range of cancer biomarkers, including CTCs, DNA fragments, and proteins.⁸¹ Owing to the unique characteristics of graphene-based nanocomposites, such as excellent electrical and thermal conductivity, luminescence, and mechanical flexibility, these thin two-dimensional nanostructures have been widely employed as bases for the detection of biomolecules and cells, proofing a promising tool for the early diagnosis of cancer.⁸² In summary, nanocomposites-based biosensors are emerging as a powerful tool for cancer diagnosis due to their enhanced sensitivity, specificity, and miniaturization compared to conventional biosensors. These biosensors integrate nanomaterials with biorecognition elements, such as antibodies, aptamers, or enzymes, to selectively detect cancer biomarkers, providing the potential to enable earlier cancer detection, improve treatment outcomes, and reduce healthcare costs.

Theragnostic Application

Nanocomposites can be designed as theragnostic agents, combining diagnostic and therapeutic capabilities. These agents can target tumors, deliver diagnostic probes, and simultaneously release therapeutic drugs, enabling real-time monitoring of treatment response and improving therapeutic efficacy.^{8,83} A study reported that a nanocomposite of DNA-templated fluorescent silver nanoclusters (AgNCs) assembled around DNA-modified gold nanoparticle (AuNP) functions as a cancer cell-specific imaging and targeted therapeutic agent. The AuNP@(AS1411-AgNCs)_n nanocomposite exhibits improved biostability, marked near-infrared fluorescence emission, and carries a high density of the first anti-cancer aptamer targeting nucleolin protein, AS1411.⁸⁴ This demonstrates the highly specific cancer cell-targeted imaging and selective killing of nanocomposites, thus potential theragnostics in the clinic. Doan and colleagues synthesized IR783 conjugated chitosan-polypyrrole nanocomposites (IR-CS-PPy NCs) as a theragnostic photoacoustic/fluorescence dual-modal imaging agent. The nanocomposite portrayed marked biosafety and near-infrared (NIR) absorbance properties with enhanced photostability. IR-CS-PPy NCs demonstrated high-efficiency MDA-MB-231 breast cancer cell ablation under NIR laser irradiation and complete killing of tumor tissues without further recurrence.⁸⁵ Thus, nanocomposites-based imaging systems could be effective theragnostic agents for imaging-guided cancer treatment. Another study found that Fe₂O₃@PPy-DOX-PEG nanocomposite can kill cancer cells and realize MRI in vivo. Mechanistically, acid stimulus

and alternating magnetic field triggered the nanocomposite to release the loaded doxorubicin hydrochloride (DOX), resulting in a remarkable combination of therapeutic effects via chemotherapy and magnetic hyperthermia and realized MRI.⁸⁶ It offers a potential alternative for the development of new nanocomposites for combination cancer therapy with MRI in vivo.

It is reported that a multifunctional nanoplatform, MFG-LPM NPs, exhibit not only MRI capacity in cancer diagnosis but also a high drug loading capacity, and integrates magnetic- and active-targeting drug delivery, light-controlled drug release, MRI, and photothermal and chemotherapy in cancer theranostics. In vivo, an MRI of tumor-bearing mice shows the nanocomposite's remarkable performance as a T2 contrast agent. In addition, in vitro cytotoxicity studies demonstrate a synergistic effect with high cancer cell-killing efficacy⁸⁷ presenting MFG-LPM NPs as an excellent theranostic agent that collectively combines multiple functions for effective MRI-guided cancer diagnosis and treatment. Fluorescent nanoparticles conjugated with a tumor-specific antibody have been used to image and target prostate cancer cells. The nanoparticles accumulate in tumor cells and emit fluorescence, allowing for the visualization of tumors.^{88,89} Theranostic nanoparticles are still under development, but they have the potential to revolutionize cancer diagnosis and treatment by providing more effective and personalized applications. The application of nanocomposites in cancer diagnosis is summarized in Table 1.

Table 1 The Diagnostic Application of Nanocomposites in Cancer

| Type of Nanocomposite | Cancer Type/Study Model | Diagnostic Technique | Key Outcomes | Reference |
|---|---|---|--|-----------|
| AuNP@(AS1411-AgNCs) _n | HeLa and NIH-3T3 cells/ in vitro | Targeted imaging and selective killing - theranostics | Specific cancer cell-targeted imaging and selective killing in a low AuNP@(AS1411-AgNCs) _n concentration | [84] |
| MFR-AS1411 | C6 rat glioma cells/ BALB/c nude mice | Targeted imaging | Specific targeting of cancer cells; enhanced fluorescence activity | [63] |
| AS1411-Au NPs/ Au@PC NP | Breast cancer/ clinical breast tissue samples | Targeted mass spectrometry imaging | Labeling agent for tumor tissue imaging by LDI-MS; binds tumor cell membranes | [64] |
| IR-CS-PPy NCs | Breast cancer/ in vitro and in vivo | Imaging and tumor-killing - theranostics | Dual-modal imaging; complete destruction of the tumor tissues with IR-CS-PPy NCs without further recurrence | [85] |
| Fe ₂ O ₃ @PPy-DOX-PEG | Hepatocellular carcinoma | Imaging and cancer cell killing - theranostics | Kills cancer cells and realizes MRI in vivo | [86] |
| ⁸⁹ Zr-Df-IAB22M2C | Metastatic melanoma, non-small cell lung cancer, and hepatocellular carcinoma/ clinical trial | Theranostics | Radiotracer uptake in tumors was noted in 10 of 15 subjects; CD8 PET imaging is safe and visualizes the whole-body biodistribution of CD8+ leukocytes in tumors and normal tissues | [71] |
| Magnetic PPy/Fe ₃ O ₄ -core and a gold nanoshell (MGNSHs) | Hela cells in vitro; Kunming mice in vivo | Multimodal imaging and photothermal cancer therapy | Enhances the contrast for both MRI and X-ray CT imaging; promising for multimodal imaging-guided cancer treatment | [65] |

(Continued)

Table 1 (Continued).

| Type of Nanocomposite | Cancer Type/Study Model | Diagnostic Technique | Key Outcomes | Reference |
|---|--|---|---|-----------|
| MFG-LPM NPs | Nasopharyngeal epidermal carcinoma cell line (KB cell), normal human embryonic lung fibroblasts (MRC-5 cell), and murine breast cancer cell line (4T1 cell); BALB/c mice | MRI-guided cancer diagnosis and therapy | Impressive MRI performance as a T2 contrast agent; high cancer cell killing efficacy | [87] |
| AuPtPd/rGO-modified GCE | Breast cancer (MDA-MB-231 and T47D cells) / in situ | Biosensor | Monitors the release of H ₂ O ₂ from cancer cells; excellent electrocatalytic activity towards the reduction of H ₂ O ₂ | [73] |
| GCE/Ti3 C2 TX / Pt-Pd/SOx | Prostate cancer/ clinical (human serum) | Biosensor | Shows potential in the early diagnosis of prostate cancer | [76] |
| SPIONs/Au/CS/SOX/NPs | Prostate cancer/ clinical (urine specimens) | Biosensor | Potential prostate cancer diagnosis via sarcosine detection | [77] |
| SarOx/CHIT/CuNPs/c-MWCNT/Au | Prostate cancer/ clinical (sera of prostate cancer patients) | Biosensor | Potential prostate cancer diagnosis via sarcosine detection | [78] |
| AuNPs/PB-PEDOT | CEA/clinical serum samples | Biosensor | Serves as an immunosensor for detecting CEA | [74] |
| SI/PEG/AuNPs/GCEs | BRCA1/clinical serum samples | Biosensor | Ultrahigh sensitivity and selectivity for BRCA1 detection | [79] |
| P[DA-β-CD/CTAB]-AgNPs-GCE | BRCA1/clinical plasma samples and MCF-7 cancer cell | Biosensor | Satisfactory results in BRCA1 detection; potential utility in clinical analysis | [80] |
| SiO ₂ @MPGs | Pancancer/ 3T3 cells, tumor-bearing mice | Biosensor | Excellent enzyme-mimic catalytic efficiency for ROS-responsive fluorescence imaging both in vitro and in vivo | [49] |
| BH-NO ₂ @BSA and BH-NH ₂ @BSA | Orthotopic hepatic tumor/ BALB/c nude mice, HCC-LM3-fLuc tumor cells | Optoacoustic tomography imaging and NIR-I/NIR-II fluorescence imaging | Capable of detecting early-stage orthotopic liver tumors | [66] |
| PSA-Mn-Msn-Cy7 | Prostate cancer/ LNCap and HSF cells, nude mice | Fluorescence and MR dual-imaging | PSA targeted-optical and MR imaging of cell and tumor-bearing mice | [88] |
| SiO ₂ @TI-RGDk NPs | Prostate cancer/ PC-3 cell, nude mice | Fluorescent imaging | Excellent targeting ability for visualizing cancer cells | [89] |

Abbreviations: AuNP@(AS1411-AgNCs)_n, gold nanoparticle@(AS1411 silver nanoclusters)nanocomposite; HeLa, human epithelial carcinoma; NIH-3T3, mouse embryo fibroblasts; AS1411-Au NPs/Au@PC NP, poly(catechin) capped-gold nanoparticles (Au@PC NPs) and smaller nucleolin-binding aptamer (AS1411) conjugated gold NPs (AS1411-Au NPs); IR-CS-PPy NCs, IR783 conjugated chitosan-polypyrrole nanocomposites; Fe₃O₃@PPy-DOX-PEG, iron(III) oxide or ferric oxide(Fe₃O₃)@ polypyrrole-(PPy)-doxorubicin hydrochloride(DOX)- polyethylene glycol (PEG); HepG2, human hepatocellular carcinoma cell line; MFG-LPM NPs, inner core of an anti-cancer drug MTX surrounding by a nanometer-thin layer of gold as the shell with Fe₃O₄ magnetic nanoparticles (NPs) evenly distributed in the gold layer, and the outermost hybrid LA-PEG-MTX molecules; AuPtPd/rGO-modified GCE, trimetallic AuPtPd nanocomposites platform on reduced graphene oxide (rGO) nanosheets with modified rGO and trimetallic AuPtPd nanoparticles on a glassy carbon electrode (GCE); GCE/Ti3 C2 TX /Pt-Pd/Sox, Ti3 C2 TX /Pt-Pd nanocomposite synthesized by a facile one-step alcohol reduction and used on a glassy carbon electrode (GCE) with sarcosine oxidase (SOx); SPIONs/Au/CS/SOX/NPs, superparamagnetic iron oxide nanoparticles (SPIONs)/gold (Au)/chitosan (CS)/sarcosine oxidase (SOX)/nanoparticles (NPs); SarOx/CHIT/CuNPs/c-MWCNT/Au electrode, sarcosine oxidase (SarOx)/chitosan (CHIT)/copper nanoparticles (CuNPs)/carboxylated multi-walled carbon nanotubes (c-MWCNT)/gold (Au) electrode; SI/PEG/AuNPs/GCEs, modified polyethylene glycol (PEG)/gold nanoparticle (AuNPs)/glassy carbon electrode (GCE); P[DA-β-CD/CTAB]-AgNPs-GCE, polymer nanocomposite-modified GCE poly(dopamine beta cyclodextrine-cetyl trimethylammonium bromide) fixed with silver NPs; SiO₂@MPGs, silicon dioxide (SiO₂)@metal crosslinked polymeric nanogels (MPGs).

Flow Cytometry Application

The integration of nanocomposites into flow cytometry has significantly enhanced its capabilities in cancer diagnostics. Flow cytometry is a valuable technique for evaluating the effectiveness of nanocomposite-based strategies. This technique is potent in analyzing the physical and chemical attributes of cells, facilitating the comprehension of the efficacy of novel cancer therapies and their response to varying environments.⁷ It often uses commercial fluorescent beads that vary in size from hundreds of nanometers to a few micrometers to enhance the sensitivity and specificity of cancer cell detection. Estévez et al designed an innovative technique for rapid and precise identification of cancer cells by employing dye-doped silica nanoparticles. Their method significantly enhanced the sensitivity of detection in flow cytometry investigations, surpassing current methods by 10 to 100 times.⁹⁰ Researchers have investigated the use of gold nanoparticles combined with other biomolecules to specifically target cancer cells. Subsequently, flow cytometry is employed to examine the fluorescence signals, enabling the detection and quantification of these cells.⁹¹ Molybdenum disulfide (MoS₂) nanocomposites have been created for the purpose of cancer diagnostics, as they possess the unique capability to selectively react to the tumor microenvironment. These nanocomposites have the ability to be combined with targeted agents and fluorescent markers, allowing for accurate identification and measurement of cancer cells utilizing flow cytometry.⁷ MoS₂-based nanomaterials can be genetically modified to selectively target cancer cells, minimizing harm to healthy cells and enhancing the safety and effectiveness of diagnostic methods.

Flow cytometry analyzes the cellular uptake, distribution, and targeting efficacy of functional nanocomposites, including those combining polymers and metallic nanoparticles, in cancer cells.⁹² Thus, nanoparticles can be engineered to transport therapeutic substances, enabling the use of both diagnostic and therapeutic functions in a single application. This not only aids in the identification of cancer cells but also facilitates the direct delivery of treatment to the specific cells, hence improving treatment results.

Nanocomposites in Cancer Treatment

Nanocomposite-Based Treatment Models/Strategies

The development of efficacious therapeutics and remedies for cancer, which ranks among the leading causes of mortality globally, is of the utmost importance. The potential of nanocomposites to facilitate the development of tailored cancer treatments lies in their distinctive characteristics. Nanocomposites have been found to possess a wide range of applications in cancer treatment, including surgery, radiation therapy, chemotherapy, etc. Nevertheless, it is imperative to thoroughly analyze the original tumor before selecting the appropriate course of treatment. Implementing nanoparticles as drug carriers has facilitated enhancements in drug kinetics, such as modulating drug and tissue interactions and prolonging circulation time.⁹³ Nanoparticles serve as passive or active vehicles by transporting drug loads, enabling them to remain undigested and preventing their elimination from the body (Figure 4). Nanomedicines incorporating nanoparticles exhibit enhanced therapeutic efficacy by selectively targeting tumor sites, immune cells, and lymph nodes.^{94,95} Concentrating therapeutic efforts within the tumor microenvironment reduces the risk of systemic exposure and unintended side effects. At the same time, the effectiveness of the treatment in the local environment is optimized. This targeted approach contributes to improved outcomes in cancer immunotherapy and surgical interventions, offering a promising avenue for advanced treatments with minimal side effects. Thus, the constraints of cancer treatment have been reduced due to the emergence of nanocarriers.

Drug Delivery Systems

Drug delivery systems (DDSs) have been investigated as an alternative method to systemic drug administration due to their ability to deliver therapeutic quantities of the drug directly to the site of the tumor in a controlled manner. DDS offers two primary benefits: first is the provision of localized drug delivery that is sustained and uninterrupted, and second is the achievement of substantial drug concentrations exclusively in the tumor microenvironment while minimizing drug levels in the bloodstream and extra-tumor tissues. Moreover, multiple material-related factors impede the effective implementation of drug delivery systems in cancer treatment, such as host immune response against the delivery system and inadequate control over drug release.⁹⁶ Research has demonstrated that DDS utilizing nanocomposites augments the therapeutic effectiveness of anticancer medications while concurrently mitigating adverse effects. A range of DDSs, including liposomes, carbon

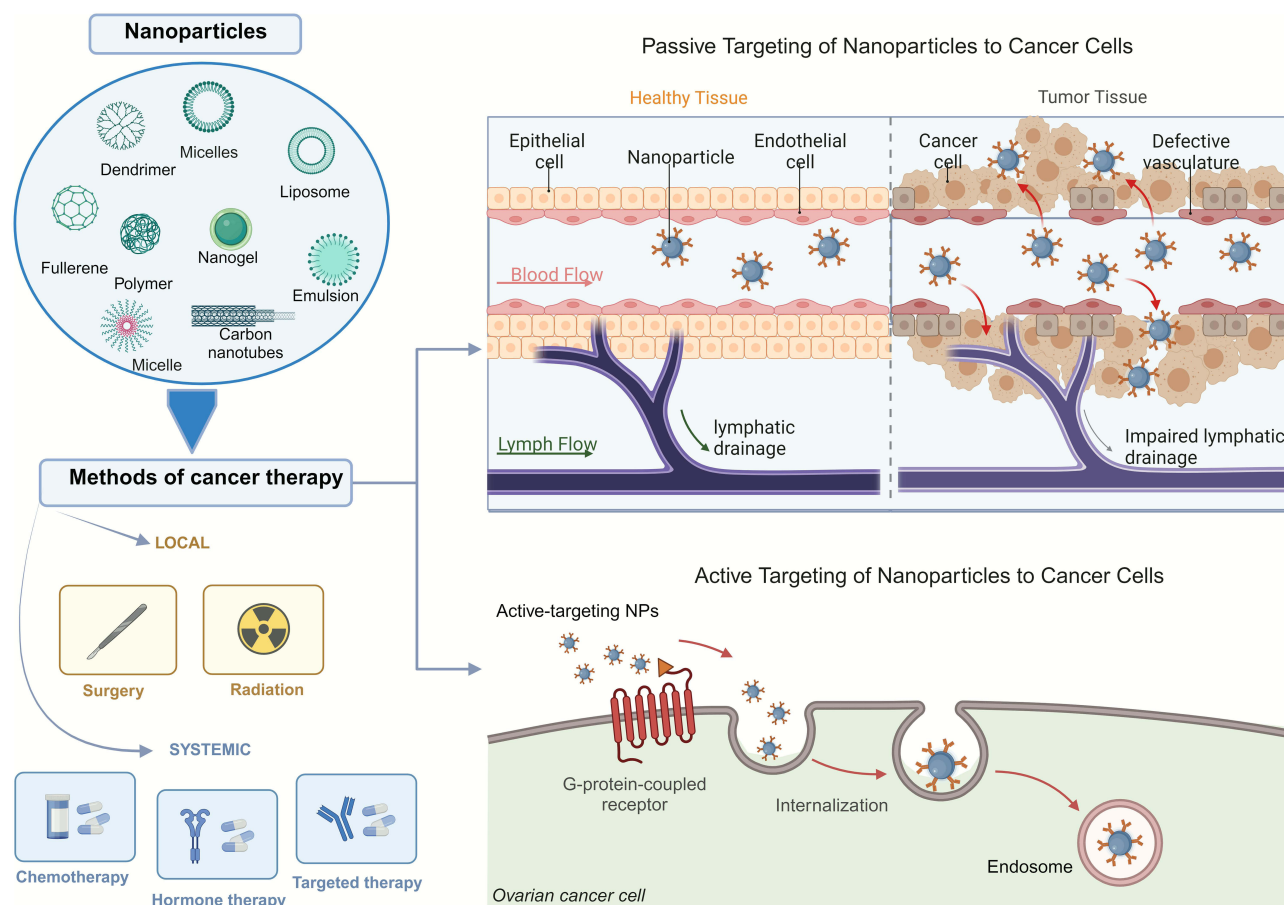


Figure 4 Targeting of nanoparticles (NPs) to cancer cells.

nanotubes, and polymeric nanoparticles, have demonstrated efficacy as carriers in cancer therapy. For example, M-MSN(Dox/Ce6)/PEM/P-gp shRNA nanocomposites exhibited a pH-responsive drug release profile. Combined photodynamic therapy and chemotherapy achieved synergistic anti-tumor effects in tumor-bearing Balb/c mice, demonstrating that tumor-bearing animals injected intravenously with these nanocomposites exhibited significant tumor uptake.⁹⁷ Nanoscale graphene oxide (nGO) encapsulated Fe_3O_4 , conjugated with folic acid (FA), and loaded with doxorubicin (DOX) (FA@ Fe_3O_4 @nGO-DOX) was a stable material used for targeted drug delivery.⁹⁸ Moreover, several challenges that have been effectively addressed in experimental and preclinical settings involving human and animal models, including insufficient tumor penetration capability, inappropriate and nonspecific tissue accumulation, premature drug release into tissues, and uncontrolled drug release at the target site, may be surmounted by employing DDSs.⁹⁹ Furthermore, they also enhance the medication's duration of action and effectiveness.

Photothermal Therapy (PTT)

With the advent of photothermal therapy (PTT), treating cancers and tumors has seen significant success. PPT employs light of specific wavelengths facilitated by photothermal absorbers.⁵ The increased heat produced by near-infrared (NIR) radiation, which induces cancer cell death, has led to the increased utilization of PTT as an alternative treatment.^{100,101} PTT is a controllable and minimally invasive method. It employs materials with high photothermal conversion efficiencies to raise the temperature of the targeted malignant sites, resulting in cancer cell death. Metal nanoparticles such as copper, gold, silver, graphene, and molybdenum have been shown to exhibit PTT.⁵ For instance, the Ion Oxide decorated MoS_2 (MoS_2 -IO-(d)PEG) nanocomposite was successfully employed to ablate 4T1 murine breast tumors.¹⁰⁰ The problem of low drug transdermal efficiency and poor efficacy of monotherapy was solved using PTT in combination with chemodynamic therapy (CDT) and chemotherapy (CT). The constructed BPMN-CuS/DOX system significantly

inhibited melanoma.¹⁰² Also, an anticancer drug, nanocomposites of the poly(N-isopropylacrylamide) (PNIPAM) containing graphene oxide (GO), PNIPAM/GO- and PNIPAMAAM/GO-based nanogels were effectively transported to cancer cells using PNIPAM/GO-DOX through the photothermal effects of NIR irradiation.¹⁰³

Photodynamic Therapy (PDT)

Photodynamic therapy (PDT), like PTT, uses optical interference. However, unlike PTT, PDT uses a therapeutic approach for triggering cell apoptosis/or necrosis that depends on singlet oxygen or other reactive oxygen species (ROS) created by photosensitizer (PS) molecules when exposed to specific light irradiation, leading to cell death.¹⁰⁴ Composite nanosystems, which combine polymer nanocarriers with embedded plasmonic metal nanoparticles and photosensitizers, are considered the most effective method for PDT in oncology. For biomedical applications, metal nanostructures must possess robust and adjustable surface plasmon resonance (SPR), exhibit little toxicity, be easily administered, and be conveniently linked to bioconjugates for targeted cancer cell interactions. Due to their robust SPR, gold nanoparticles (GNPs) are consistently evaluated for their potential application in PDT.¹⁰⁵ In PDT, the ability of GNPs to absorb light and convert it into heat can be utilized to either release a chemical payload by inducing heating or generate ROS to cause cellular necrosis or apoptosis at targeted tumor sites.¹⁰⁶ For instance, by integrating lactate oxidase (LOx) and catalase (CAT) into iron oxide (Fe_3O_4) nanoparticle/indocyanine green (ICG) co-loaded hybrid nanogels, toxic ROS were produced by endogenous hydrogen peroxide (H_2O_2) at the tumor site, resulting in the death of cancer cells even without the presence of external oxygen (O_2).¹⁰⁷ In addition, a porphyrin-based nanoscale metal-organic framework (NMOF), DBP-UiO, was used as PS for PDT. This chlorin PS functionalized with DBC-UiO demonstrates a redshift of 13 nm and an 11-fold increase in the extinction coefficient of the lowest-energy Q band. This results in more efficient singlet oxygen production ($^1\text{O}_2$) and considerably improves the efficacy of PDT.¹⁰⁸

Gene Therapy

In emergent cancer therapies, gene therapy (GT) represents a method by which targeted tumor cells are injected with genes that either overexpress oncogenic proteins or promote apoptosis. Gene therapy encompasses the processes of gene transduction, gene stability maintenance, and complete gene expression. The precision of gene replacement strategies is enhanced by the targeted and efficient delivery of therapeutic genes made possible by nano-delivery systems.¹⁰⁹ In gene therapy, nanocomposite delivery systems provide targeted drug delivery and enhanced treatment efficacy, offering several benefits in cancer treatment, including heightened specificity, diminished adverse effects, and improved therapeutic efficacy.¹¹⁰ The material must possess two critical characteristics for gene delivery applications: compact size and the capacity to interact with genetic material, forming a durable complex.¹¹¹ Efforts have been devoted to developing carriers that effectively compact and safeguard oligonucleotides for gene therapy. In cancer treatment, microRNA (miRNA)-based therapies have demonstrated encouraging outcomes; furthermore, the application of nanocarriers to deliver miRNA can augment their therapeutic effectiveness. In various preclinical cancer treatment studies, nanocomposites of polymers and lipids have been assessed for their ability to inhibit dysregulated cytokines and impede tumor growth. Several primary categories of nanocarriers have been employed to transport miR34a in the context of cancer therapy. A recent study used a lipid-based nanoparticle formulation to deliver a small molecule inhibitor of the protein CK_2 to treat pancreatic cancer. The lipid-based nanoparticles were found to have the CK_2 inhibitor to the tumor site in an effective manner and to inhibit CK_2 activity to a significant degree, exhibiting no discernible toxicity or intolerance in the mice.¹¹² In another study, researchers employed mesoporous silica nanoparticle (MSN)-based drug delivery systems to treat breast cancer.¹¹³ They used MSNs loaded with the chemotherapy drug doxorubicin (DOX) and conjugated them with a tumor-targeting peptide called iRGD.

Key Nanocomposite-Based Materials in Cancer Treatment

Nanocomposites, including carbon-based nanocomposites,¹¹⁴ polymeric nanocomposites,¹¹⁵ metal-based nanocomposites,¹¹ lipid-based nanocomposites,¹¹⁶ hybrid nanocomposites,¹¹⁷ and ceramic nanocomposites,¹¹⁸ have garnered significant interest for treating prominent cancers (Figure 5 and Table 2). The emergence of these materials has enabled the comprehension of cellular mechanisms within living cells and the development of technologies that aid in the timely detection and management

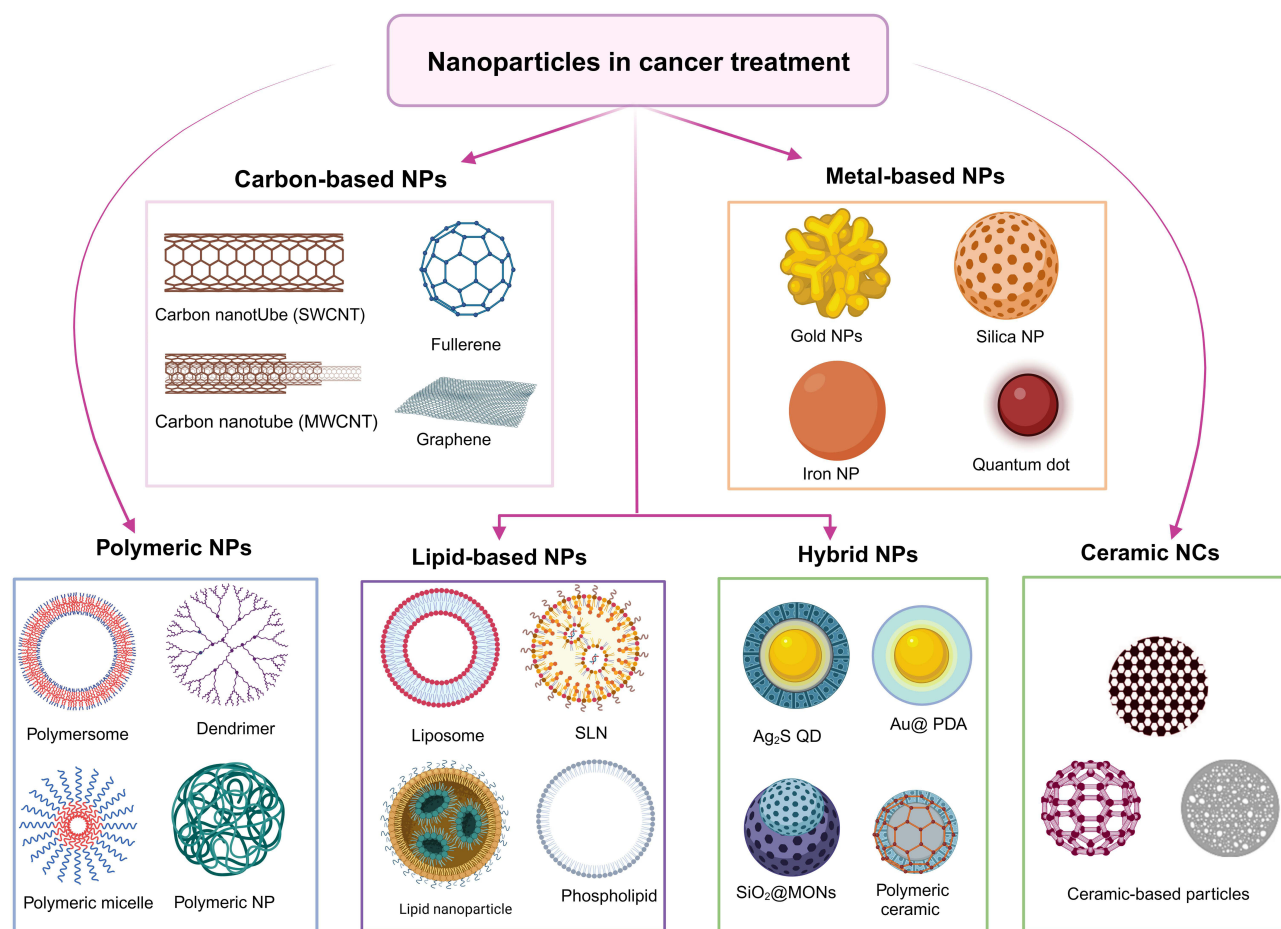


Figure 5 Examples of the nanoparticles (NPs) used in nanocomposite composition for therapeutic management of different types of cancers.

Abbreviations: SLN, solid-liquid nanoparticle; Ag₂S QD, silver sulfide quantum dots; Au@PDA, gold coated with polydopamine; SiO₂@MONs, silicon dioxide with microporous organic networks.

of diverse diseases. The ultimate goal of cancer therapy, as is well known, is to selectively target tumor cells while avoiding harm to adjacent healthy tissues. Nanocarriers enhance the therapeutic efficacy of anticancer medications and facilitate selective accumulation at their intended site.

Nanocomposite-based drug delivery systems have been demonstrated to enhance the therapeutic efficacy of anticancer treatments and reduce side effects. Nanocomposites offer several advantages over small-molecule drugs or medications. These include precise or targeted delivery to specific cells or tissues, minimizing off-target effects.¹²⁹ In terms of size and composition, they are in the nanometer size range and have unique compositions that confer them superiority over conventional materials.¹²⁹ Moreover, tailored applications¹³⁰ allow for the customization of polymeric nano-biocomposites for sustained and targeted drug delivery applications, providing customized solutions for specific medical needs. Nanocomposites have superior nanostructures, enhancing drug transport effectiveness.¹³¹ They ensure site-specific delivery and precise medicines for treating chronic human diseases.¹³² Additionally, nanocomposites have a high capacity to encapsulate a large amount of drug internally or on their capacity, which exhibits an increased capacity to encapsulate a large amount of drug internally or on their surface, enhancing drug delivery efficiency.¹³³ As a result, numerous varieties of nanocarriers, including polymers, micelles, dendrimers, mesoporous silica nanoparticles, liposomes, and nanosized metal-organic frameworks (nMOFs), have been developed for cancer treatment.⁹⁵

Carbon-Based Nanocomposites

Carbon-based nanocomposites integrate a carbon-based substance (such as carbon nanotubes, graphene, or fullerenes) with another substance at the nanoscale. The combination frequently yields improved characteristics in comparison to the

Table 2 Types of Nanocomposites Used in Cancer Treatment

| Type of Nanocomposite | Cancer Type/Study Model | Treatment Method | Key Outcomes | Reference |
|--|---|----------------------------|--|-----------|
| CuInS ₂ /ZnS/liposome-rGO (Carbon-based nanocomposite) | Human esophagus carcinoma cells. In-vitro: Eca-109 cells; In-vivo: Mice | PTT and PDT | Reduced the toxicity caused by CuInS ₂ /ZnS | [119] |
| DOX-GO-PEG-FA (Carbon-based nanocomposite) | Melanoma. In-vitro: B16F0 cells; In-vivo: male C57BL/6 J mice | PTT and PDT | GO-PEG-FA initiates the generation of singlet oxygen required to demonstrate dual-mode photodynamic and photothermal treatment in-vivo for the treatment of tumors upon NIR light activation | [120] |
| PLGA-TPGS (Polymeric nanocomposite) | Human breast adenocarcinoma/ MCF-7 cell line | CT | Induced apoptosis/overcome multi-drug resistance | [121] |
| MPEG-PCL (Polymeric nanocomposite) | CT26 mouse colon carcinoma cell line | CT | Sustained the release of the drug | [122] |
| mTiO ₂ @PPY (Metal-based nanocomposite) | Human hepatoma HepG2/4T1 cell lines | PTT/SDT/CT | Synergistic antitumor therapy | [123] |
| Fe ₃ O ₄ @Bio-MOF-FC (Metal-based nanocomposite) | Lung carcinoma (M109)-bearing BALB/c mice | DDS | Tumor shrinking | [124] |
| MoS ₂ -PEI-HA (Lipid-based nanocomposite) | Mice bearing MCF7-ADR tumor | DDS | Completely eradicate tumor | [125] |
| DOX@MoS ₂ -PEI-HA (Hybrid nanocomposite) | Metastatic breast cancer | PTT | Significantly enhanced breast tumor growth inhibition | [126] |
| TiONts-AuNPs-PEG3000-DTX (Hybrid nanocomposite) | Human PC-3 prostate adenocarcinoma cells | IT injection/ radiotherapy | Delayed tumor growth | [127] |
| FePt@Kao-Dox (Ceramic nanocomposite) | Hepatocellular carcinoma | CT | Enhances magnetic signal and killing of tumor cells | [128] |
| SCPC (Ceramic nanocomposite) | Breast cancer/ 4T1 mammary tumor cells | DDS | Stopped tumor growth | [96] |

Abbreviations: CuInS₂/ZnS/liposome-rGO, Copper Indium sulfur zinc sulfide/liposome on reduced graphene oxide; PTT, photothermal therapy; PDT, photodynamic therapy; DOX-GO-PEG-FA, Doxorubicin-Graphene Oxide-Polyethylene Glycol-Folic Acid; B16F0 cells, murine melanoma cell line; PLGA-TPGS, poly(lactide-co-glycolide)-d-a-tocopheryl polyethylene glycol 1000 succinate; MCF-7 cell line, Michigan cancer foundation-7 cell line; MPEG-PCL, Methoxy Poly(ethylene glycol)-Poly(ε-caprolactone); SDT, sonodynamic therapy; CT, chemotherapy; mTiO₂@PPY, mesoporous TiO₂ coated with polypyrrole; Fe₃O₄@Bio-MOF-FC, Bio-Metal-Organic Framework coated with folic acid-chitosan conjugate; MoS₂-PEI-HA, Molybdenum Disulfide (MoS₂) - Polyethyleneimine (PEI) - Hyaluronic Acid; MCF7-ADR, Multidrug-resistant MCF-7 breast adenocarcinoma cells; DDS, drug delivery systems; DOX@MoS₂-PEI-HA, doxorubicin molybdenum sulfide-polyethyleneimine-hyaluronidase; TiONts-AuNPs-PEG3000-DTX titanate nanotubes-gold nanoparticles-heterobifunctional polymer-docetaxel; FePt@Kao-Dox, Iron/Platinum-Based Kaolinite- doxorubicin; SCPC, silica-calcium phosphate nanocomposite.

individual constituents. They possess exceptional mechanical strength, electrical conductivity, thermal conductivity, barrier characteristics, and chemical resistance. These devices are cleverly developed and constructed to improve the effectiveness of drug delivery in cancer treatment. Carbon-based nanocarriers are the most commonly used in the delivery field due to their unique properties, which include binding to the cell membrane, which provides the optimal environment for DOX release, and triggering cell membrane ruffling, which induces cell stress and ultimately results in methuosis, apoptosis, and ROS production.¹³⁴ Carbon nanotubes, due to their hydrophobic hollow interior, facilitate the loading of water-insoluble drugs, making them promising for delivering tumor-treating medications. Carbon nanotubes (CNTs) are classified as single-walled carbon nanotubes (SWCNTs) or multi-walled carbon nanotubes (MWCNTs)¹³⁵ In addition, they are sensitive to PET and MRI. Graphene and its nanocomposites have recently been widely used in

biomedicine for cancer therapy. Also, graphene, which is lipophilic, can help in membrane barrier penetration. As nanocarriers, reduced graphene oxide (rGO) and MWCNTs enhance cellular permeability and loading capacity.¹³⁶

Polymeric Nanocomposites

Polymeric nanocomposites are a class of nanocomposite materials in which at least one of the phases consists of a polymer. Nanoparticles, usually smaller than 100 nm, are dispersed within a polymer matrix to form them. These blends frequently result in substantial character enhancements compared to conventional polymer materials. Polymeric nanocomposites have notable characteristics, including facile synthesis, biocompatibility, non-toxicity, non-immunogenicity, biodegradability, and tailored drug administration, rendering them favored theranostic tools.¹³⁷ Some commonly used polymeric nanoparticles are polymersomes, polymeric micelle, and dendrimers. Polymersomes are polymeric self-assembled vesicles prepared using amphiphilic block copolymers with a hydrophobic bilayer encapsulating an aqueous core.¹³⁸ As such, polymersomes are gaining popularity as theranostic nanoparticles due to their expanding applications as platforms for simultaneous drug delivery and imaging. Polymeric micelles, another amphiphilic block copolymer, have been used as delivery vehicles for hydrophobic agents.¹³⁸ PLA-based micelles were created to load Ruthenium (Ru) for improved cancer treatment. The micelles consisted of MPEG-SS-PMLA, which is a combination of poly(ethylene glycol) and phenyl-functionalized poly(lactic acid) connected by a disulfide connection. The MPEG-SS-PMLA contained approximately 83% Ru content, which was attributed to the π - π bonding between the phenyl ring and the Ru complex. At a concentration of 10 mmol/L, under the influence of GSH, 70% of Ru was released, leading to apoptosis in MCF-7 cells.¹³⁹ Dendrimers are tree-like, three-dimensional macromolecules that are exceptionally branched. Their considerable surface area facilitates the affixed of many functional groupings, imparting versatility across various applications. Recently, there has been considerable interest in cancer research regarding dendrimer-based drug delivery. This interest stems from the branched structure and abundant functional group terminations present in dendrimer polymers, which enhance the efficiency of drug encapsulation and conjugation. Consequently, numerous biologically active molecules, including chemotherapeutic medications and MRI contrast agents, were successfully delivered via dendrimers.^{140,141}

Metal-Based Nanocomposites

Metal-based nanocomposites combine a metal or metal oxide with other materials at the nanoscale. Their properties can be customized by varying the type of metal, the matrix material, and the fabrication process. They exhibit enhanced strength, toughness, stiffness, thermal and electrical conductivity, and resistance to corrosion, wear, and heat.¹⁴² There has been a growing fascination with magnetic nanoparticles, which can potentially be used for disease diagnosis and treatment. The primary concept is to regulate the targeted distribution of these nanoparticles solely through utilizing the magnetic field. Photothermal therapeutic agents can utilize metal particles. For example, functionalized gold nanoparticles (AuNPs) are highly suitable for delivering novel therapeutics due to their remarkable biocompatibility and predictable bioavailability.^{143,144} The predominant application of iron oxide nanoparticles is in cancer therapies based on magnetic spin, in which oxygen radicals are generated to detect the presence of cancer. Furthermore, these nanoparticles can induce local toxicity ROS and reactive nitrogen species for tumor therapy and are remotely controllable via an external electromagnetic field. This type of treatment produces fewer adverse effects in healthy and normal tissues. The capability of remotely controlling iron oxide nanoparticles laden with antitumor drugs confers additional benefits compared to conventional antitumor drugs.¹¹

Lipid-Based Nanocomposites

Lipid-based nanocomposites, also known as lipid-based nanoparticles, are materials that blend lipids (oils or fats) with other elements to form structures possessing distinctive functions and properties. Lipids are endogenous to the body, rendering them inherently biocompatible and reducing the likelihood of eliciting unpleasant reactions. They can be engineered to selectively target particular cells or tissues, augmenting treatments' effectiveness and minimizing adverse reactions. Additionally, they can encapsulate and safeguard pharmaceuticals or other compounds, allowing for regulated discharge either gradually or at particular locations within the body. Liposomes have emerged as the preferred drug delivery vehicle due to their extensive clinical history and firmly established attributes. For instance, stealth liposomes coated with polyethylene glycol (PEG) demonstrated improved blood circulation time for 2–3 days following intravenous administration.¹⁴⁵

Hybrid Nanocomposites

Hybrid nanocomposites are materials formed by synthesizing two or more distinct components at the nanoscale, often involving one organic and one inorganic component. This combination frequently leads to improved characteristics in the resulting hybrid material, which neither component could individually attain.¹⁴⁶ Titanate nanotube (TiONT) nanohybrids were created to combat prostate cancer using intratumoral (IT) injection. Before use, the surface of TiONts was pre-coated with a siloxane called APTES. This coating allowed for the attachment of both dithiolated diethylenetriamine-pentaacetic acid-modified gold nanoparticles (Au@DTDTPA NPs) and a heterobifunctional polymer called PEG3000. The purpose of this coating was to greatly enhance the stability of the suspension and the compatibility of TiONts for specific biomedical applications.¹²⁷

Ceramic Nanocomposites

Ceramic nanocomposites are advanced composite materials that merge ceramics with reinforcing elements at the nanoscale, enabling the customization of material properties to suit specific applications. This combination yields materials with enhanced characteristics, including decreased weight compared to conventional ceramics, greater strength, dimensional stability, and heightened resistance to heat, wear, and tear.^{147,148} For instance, bioceramics are ceramic materials compatible with living tissues, making them suitable for medical and dental implants. Bioactive magnesium silicate ceramics are predominantly assessed in bone tissue engineering. This is owing to their exceptional mechanical characteristics and capacity to induce cellular adhesion, proliferation, and differentiation, consequently facilitating more rapid bone regeneration than traditional bioceramics. As a result of their superior mechanical properties and accelerated bone regeneration, magnesium silicate-based bioactive ceramics (Mg_2SiO_4) have been evaluated in bone tissue engineering for their ability to stimulate cell adhesion, differentiation, and proliferation.¹⁴⁹ Calcium-phosphate ceramics have been explored as a delivery medium for antibiotics, proteins, steroids, hormones, anticoagulants, and anticancer medications.¹⁵⁰ Also, the sustained release capabilities of hydroxyapatite (HA) and tri-calcium phosphate (TCP) porous blocks for anticancer medications, such as methotrexate and cisplatin, have been assessed.⁹⁶

Improving Targeted Cancer Therapies

Nanomaterials typically have dimensions ranging from 1–100 nm. Because of their small sizes, they can interact distinctively with tissues and cells, making them viable candidates for cancer therapy and drug delivery. These nanoscale features give them distinct optical, electrical, and magnetic capabilities. The integration of nanotechnology and cancer treatment presents an opportunity to enhance the effectiveness of therapeutic agents, mitigate unintended harm to benign cells, and improve patient prognoses.¹⁵¹ Additionally, it is possible to modify nanomaterials to target a moiety specifically. Targeted delivery is a significant advantage of nanomaterial-based cancer therapy over free drugs. Targeted drug delivery systems reduce cell toxicity by delivering drugs selectively and directly into cells. Nanomaterial-based drug delivery systems have reflected cancer treatment and management benefits by demonstrating precise targeting, good pharmacokinetics, reduced side effects, and drug resistance.^{152,153} Nanoparticle drug delivery systems, characterized by their ability to achieve accurate targeting and exhibit favorable pharmacokinetics, play a significant role in enhancing the efficacy of cancer treatment.¹⁵⁴ Furthermore, their modifications are designed to selectively affect cancer cells, the immune system, and the tumor microenvironment (TME), expanding the range of potential cancer treatments.

Diverse forms of nanotechnology, such as lipid-based nanomaterials, polymeric nanoparticles, liposomes, carbon nanomaterials, etc., have been utilized in cancer therapy. These materials have improved drug delivery to cancer cells, reduced toxicity to healthy cells, and improved patient outcomes.¹⁵⁵ Using intricate design and modification, nano-drugs can effectively address the drawbacks associated with conventional chemical therapy by virtue of their enhanced specificity, bioavailability, reduced cytotoxicity towards normal tissue, increased loading capacity, prolonged half-life, and distinctive drug release patterns. Research highlights the potential of carbon nanomaterials in cancer treatment, including graphene and fullerene, demonstrating continuous advancements in this domain.^{156–158} Recently, there has been a growing interest in applying graphene-related nanomaterials to photothermal therapy. Graphene oxide (GO) has been shown in multiple studies as a drug nanocarrier capable of enhancing cancer-targeting drug release profiles, facilitating chemotherapy cellular uptake and accumulation in cancer cells, and mitigating chemotherapy's adverse

effects on normal cells.¹⁵⁹ Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibited immune responses as an immune checkpoint blockade in cancer immunotherapy.¹⁶⁰ Notwithstanding the vast array of nanomaterials developed to target cancer, only a restricted selection of liposomes and polymer nanoformulations have obtained clinical approval. For instance, long-circulating polymeric nanoparticles have been developed with diblock copolymers composed of PEG and biodegradable polymers like PLGA. Liposomes have been enhanced by the drug delivery field to transport chemotherapeutic agents to tumors effectively, resulting in an improved therapeutic index and decreased adverse effects.¹⁶¹

Progress and Advancements

Recent Advances in Nanocomposite-Based Cancer Diagnosis

Cancer diagnosis plays a pivotal role because it entails the specific identification of a tumor within the body and the assessment of its size in order to determine whether it is in its early stages or a case of recurrence. Nanocomposites have emerged as a frontiering domain in the realm of cancer diagnosis, presenting novel methodologies to augment both detection and therapeutic interventions. In recent years, substantial progress has been made in utilizing nanocomposites for cancer diagnosis. Using nanocomposites in diagnostic applications introduces novel approaches that improve accuracy and sensitivity.

Electrochemical biosensors have recently attracted much attention due to their extraordinarily high selectivity, sensitivity, and affordability in early cancer diagnosis. Nanocomposite biosensors are being developed for non-invasive cancer detection using readily available fluids such as blood or saliva, holding enormous promise for early diagnosis. Biosensors comprised of nanocomposites, including graphene and MoS₂, have been developed to provide label-free diagnosis of cancer cells and biomarkers with exceptional precision.^{7,162} Also, functionalized nanoparticles have a high affinity for specific cancer biomarkers, such as proteins and nucleic acids, allowing for sensitive detection and accuracy, which is vital in improving patient outcomes.⁹¹ Nanocomposite-based microfluidic devices can efficiently capture and analyze rare circulating tumor cells (CTCs) from blood, enabling early detection of metastasis and treatment monitoring.¹⁶³ Functionalized DNA nanostructures have a significant role in cancer diagnosis. These structures function as adaptable platforms for biosensors and other diagnostic instruments, demonstrating the potential of DNA-based nanomaterials in oncology. Chen and Seeman presented 3-D organized DNA in 1991,¹⁶⁴ with the DNA tetrahedron gradually becoming a typical 3D structure after development and simplification; it still plays essential roles in detection and analysis applications and drug carriers. More recently, a group of researchers synthesized DNA-templated silver nanoclusters (DNA AgNCs) by utilizing a multi-branched linear (MBL) DNA structure that was generated through a triggered hybridization chain reaction (HCR). The DNA AgNCs, assembled using the MBL structure and attached to aptamers targeting cancer cells, demonstrated a detection sensitivity approximately 20 times higher than DNA AgNCs attached to individual aptamers.¹⁶⁵

Recent Advances in Nanocomposite-Based Cancer Treatment

Nanomaterial-based cancer treatment has demonstrated advantages over free drugs, especially in targeted delivery.¹⁶⁶ In the past decade, there has been exciting improvement in nanocomposite-based cancer treatment. As a result of their substantial surface-area-to-volume ratios and nanoscale dimensions, nanocarriers can positively impact the basic properties and biological functions of their payloads. Nanocomposites can improve the effectiveness of immunotherapy and decrease the overall exposure of the drugs to the body. Favorable characteristics of nanocomposites often encompass their capacity to transport multiple loads, safeguard therapeutic agents throughout delivery, profoundly penetrate malignant tissue, and enable targeted administration to specific sites.¹⁶⁶ This approach has the potential to overcome drug resistance and improve treatment outcomes. Lipid-mediated and polymer-mediated nanoformulations of anti-cancer medications, combined with nanotherapy in drug delivery, have substantially enhanced targeted drug delivery, augmented therapeutic efficacy, and minimized adverse effects on healthy cells.¹⁶³ Nanoparticles can be modified by targeting ligands that selectively identify and adhere to cancer cells, transporting the therapeutic payload directly to the tumor location while limiting harm to healthy organs. The latest advancements in nanosystems based on layered double hydroxides (LDHs) demonstrate their considerable potential as effective instruments in the field of cancer therapy.

These nanocomposites provide diversity and efficacy in therapeutic drug delivery.¹⁶⁷ As carriers for delivering therapeutic genes to cancer cells, gene therapy nanocomposites present a promising avenue for personalized medicine and treating cancer-associated genetic mutations. This technology exhibits significant promise in advancing innovative cancer therapies with enduring impacts.¹⁶³ Stimulus-responsive nanocomposites are likewise engineered to exploit particular stimuli in the tumor microenvironment, such as pH, temperature, or enzymatic activity, to liberate their therapeutic substratum. By implementing a controlled release mechanism, the effectiveness of the substance can be increased while potential adverse effects are reduced.¹⁶³ As ongoing research in this domain advances, it is foreseeable that further groundbreaking and efficacious therapeutics will surface, presenting a glimmer of hope for enhanced patient prognoses and, conceivably, cancer cures.

Regulatory Considerations for the Clinical Translation of Nanocomposites

Although the clinical translation of nanocomposites for therapeutic applications opens up new avenues for customized medicine and better patient outcomes due to the unique features and possible hazards connected with nanoparticles, it also needs careful consideration of numerous regulatory challenges. Firstly, safety and efficacy should be considered. Concerns, including the thorough characterization of the nanocomposite, assessment of its potential toxicity, mechanisms of biodistribution, and clearance methods, are crucial to consider. Various regulatory bodies, including the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA), have established precise criteria for evaluating the safety and effectiveness of nanomedicines. These requirements frequently necessitate comprehensive information regarding the manufacturing process, quality control protocols, and characterization of the physicochemical properties of the nanocomposite.¹⁶⁸ In addition, manufacturing and quality control are essential. Another area to be considered is the risk-benefit assessment. The ability to reliably and at scale create nanocomposites for clinical studies and possible commercialization is critical. Regulatory bodies need stringent quality control methods to assure batch-to-batch uniformity and reduce any variability in the medicinal product. Furthermore, it is essential to ascertain the nanocomposite's precise dimensions, shape, surface characteristics, and composition to maintain consistent quality and monitor potential safety issues. Regulatory authorities may demand extensive documentation of the manufacturing process and batch release criteria.^{168,169}

Regulatory bodies balance the potential benefits of a nanocomposite-based therapy against the reported hazards, considering aspects such as disease severity, current treatment choices, and possible adverse effects. This evaluation aids in determining the regulatory pathway and approval requirements for clinical trials and market authorization. Strategies for risk reduction are another area to contemplate. It is critical for regulatory approval to identify and mitigate any risks connected with the nanocomposite, such as immunological response, off-target effects, or environmental impact. Also, ethical behavior is an essential aspect to consider. Informed permission is necessary for involvement in clinical trials employing nanocomposites. Patients should be fully informed about the therapy's possible dangers and benefits, including the uncertainty related to nanomaterials. Building trust and acceptance requires open communication; therefore, transparency and communication with the patients, healthcare professionals, and the general public regarding nanocomposite-based medicines' development and potential hazards.¹⁷⁰ The regulatory framework for nanocomposites in clinical translation is complicated, but it is critical for guaranteeing the safety and efficacy of these exciting novel medicines. Researchers and developers can boost the likelihood of successful clinical translation and deliver the benefits of nanocomposite-based drugs to patients by proactively addressing these factors and collaborating with regulatory regulators.

Ongoing Clinical Trials and Their Outcomes

Current clinical studies in cancer nanotechnology investigate several strategies, such as nanomedicines and nanocomposites. Cancer treatment utilizing nanocomposites is advancing rapidly, with several active clinical trials evaluating the safety and efficacy of these innovative medications. Nevertheless, the intricate structure of nanomaterials poses difficulties in their manufacturing and quality control processes, which often require optimization based on additional clinical discoveries. Preliminary results from ongoing clinical trials exploring the application of nanocomposite-based cancer therapy demonstrate promising outcomes in terms of safety, tolerability, and potential efficacy. Research

emphasizes the importance of these trials in enhancing cancer diagnosis and therapies. Significantly, specific trials prioritize the use of combination immunotherapy to augment treatment results. Although pre-clinical studies have shown encouraging outcomes, additional research is necessary to convert these findings into practical use in clinical settings.

A new era for the use of nanoparticles in various chemotherapies began with the FDA's 1995–1996 approval of liposomal and PEG-conjugated doxorubicin and 2005's approval of albumin-nanoparticle conjugated paclitaxel.¹⁷¹ Nanoparticles, particularly those made of polymers responsive to ultrasound, demonstrate efficacy in detecting and treating cancer. Also, several liposomal nanoparticle (NP) therapies have progressed in clinical trials for various cancers. For instance, Onivyde (liposomal irinotecan) has completed Phase I/II trials for metastatic breast cancer. BIND-014 (PSMA-targeted polymeric NPs) has completed Phase I/II trials for KRAS-positive/squamous cell NSCLC and metastatic castration-resistant prostate cancer. Vyxeos (liposomal NPs co-delivering cytarabine and daunorubicin) is FDA-approved and in Phase I/II trials evaluating combinations with other drugs for leukemia.¹¹⁶ The efficacy and safety of combining motolimod, pegylated liposomal doxorubicin, and durvalumab (an immune checkpoint inhibitor) were investigated in Trial NCT02431559 (completed Phase I/II) (data collected from ClinicalTrials.gov). The study focused on participants with platinum-resistant ovarian cancer who had undergone at least two rounds of chemotherapy before the trial. The trial results demonstrated that the combination exhibited favorable tolerability and superior efficacy compared to monotherapies. These trials have shown that combining immune checkpoint inhibitors, chemotherapy drugs, and nanocomposites may extend the time patients with various cancers live without their disease worsening.

Challenges and perspectives

Challenges and Future Directions of Nanocomposite-Based Cancer Diagnosis

While nanocomposites have enormous potential to revolutionize cancer diagnostics, they also face distinct challenges and fascinating prospects. Concerns about reliability are a fundamental challenge in assuring the dependability of nanotechnology-based systems in cancer diagnosis. Consistent and precise results are critical for practical application.¹⁷² Although nanoparticle-based drug delivery systems show promise in cancer treatment, precision targeting needs further improvement to improve efficacy and avoid off-target effects.¹⁵⁴ In addition, current research in MoS₂-nanocomposites focuses on biosensors, bioimaging, and therapeutic applications. Overcoming these obstacles is critical for progressing cancer diagnosis and therapy.⁷ Future directions include creating safe nano-based materials for cancer detection; thus, the safety of these materials is critical for clinical applications. Innovative nanomaterials for cancer theranostics encounter obstacles that must be addressed before they can be successfully integrated into clinical practice.⁴² Addressing reliability difficulties, improving precise targeting, producing safe nanomaterials, and overcoming theranostics challenges will pave the road for nanocomposite-based cancer diagnostics to become more reliable and successful. However, to tackle the obstacles successfully and take full advantage of the promising prospects of nanocomposite-based cancer diagnostics, researchers, clinicians, and engineers must work together collaboratively.

Challenges and Future Directions of Nanocomposite-Based Cancer Treatment

Unique and effective ways are being explored for targeted drug delivery, increased therapeutic efficacy, and fewer side effects in nanocomposite-based cancer treatment. However, significant difficulties must be overcome before these therapies are routinely used in clinical practice. For instance, maintaining high sensitivity while designing nanocomposites that can reliably distinguish cancerous from healthy cells remains a challenge. False positive and negative results may result in inappropriate treatment decisions and misdiagnoses. The extensive diversity among cancer types underscores the need to create adaptable nanocomposites that detect distinct tumor attributes and mutations. One-size-fits-all strategies are improbable to achieve success. Moreover, incorporating nanocomposites into established imaging modalities such as ultrasound or MRI necessitates meticulous deliberation regarding compatibility, safety, and signal amplification. These factors can be challenging to balance. Before their widespread clinical application, prospective long-term safety concerns regarding the biocompatibility and toxicity of nanocomposites must be exhaustively addressed. Not forgetting the imperative to ensure the accessibility and practical implementation of nanocomposite-based diagnostic instruments in healthcare settings necessitates the development of scalable and cost-effective manufacturing processes.

Nanocomposites have immense potential to transform the field of cancer diagnostics and treatment. The present state of research offers valuable insights into the prospects of utilizing nanocomposites in clinical development within this field. Further refinement of these therapies, optimization of delivery systems, and investigation of synergistic combinations with other treatment modalities will be the focus of ongoing and forthcoming clinical trials. Future endeavors are centered around improving nanocomposites for specific cancer treatment, aiming to increase treatment accuracy and minimize adverse effects. Nanoparticles are proposed as a remedy to address drug resistance, a prevalent obstacle in chemotherapy. The objective of nanocomposite design is to enhance the efficacy of treatment. The exploration of nanocomposites, specifically the use of MnO_2 nanoparticles to generate oxygen and alleviate tumor hypoxia, is being studied to hinder the proliferation and migration of cancer cells. Scientists are developing customized treatments using nanomaterials, considering specificity, cytotoxicity, and drug capacity parameters.^{7,25,151,166,173} With the advancement of research, it is foreseeable that in the near future, nanocomposite-based cancer treatments will become more productive and secure.

Conclusion

The rise in cancer cases has led to the rapid advancement of many diagnostic and therapeutic agents, including proteins, peptides, and small molecule cytotoxic drugs, hence broadening the range of cancer diagnosis and treatment options. The advancement of nanotechnology has led to many self-adaptive nanomaterials designed explicitly for bioactive particle delivery. Thus, nanotechnology-based therapy and diagnosis represent an innovative strategy aimed at advancing the clinical management of cancer while mitigating the limitations associated with presently accessible models. By strategically creating nanoparticles, researchers can deliver drugs to specific cell populations, the tumor site, or even difficult-to-access tissue compartments, thereby reducing the potential for adverse effects on healthy tissues and organs. The fabrication of responsive and multifunctional composite systems is facilitated by functionalizing inorganic nanoparticles using biocompatible polymers and biomolecules, whether naturally occurring or synthetic. Targeted nanocomposites ensure drug delivery to the desired tissue, cell, or organ (subcellular targeting), enhancing accuracy, efficacy, and adverse effect mitigation. By minimizing drug elimination from the system, these nanosystems employ both passive and active delivery to tumor areas. Despite the limited number of human clinical trials that have commenced thus far, nanocomposite materials composed of functionalized semiconductors and metal nanoparticles can fundamentally transform the methods employed in detecting and treating cancer. It is crucial to acknowledge that although obstacles and ambiguities exist, continuous research and optimization endeavors concerning the utilization of nanocomposites present a prospect to tackle these issues and facilitate the development of cancer diagnoses and treatments that are both safer and more efficient.

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