### **Cancer Insight**



### **Review Article**

## Advances in the Use of Nanomaterials in Tumour Therapy: Challenges and Prospects

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#### ABSTRACT

Nanomaterials have shown great potential in anti-tumor applications and are currently the focus of research. This review article aims to provide a comprehensive overview of the challenges encountered in oncology treatment and how nanomaterials are being utilized to overcome these obstacles. The authors discuss the limitations of conventional treatments, including limited efficacy, side effects, and toxicity issues. They highlight the importance of early tumour diagnosis and personalized treatment plans, as well as the need for innovative therapeutic approaches such as targeted therapy, immunotherapy, and gene therapy. The article primarily focuses on how nanomaterials can be engineered to achieve specific recognition and aggregation within tumour tissues through surface modifications involving targeting molecules such as antibodies, peptides, and receptor ligands. This surface modification technique facilitates improved targeting in the targeting of photodynamic therapy, while minimizing harm to normal tissues. The authors also discuss the potential and future prospects of nanomaterials in tumour therapy, including breakthroughs in their application, biosafety concerns, biocompatibility issues, preparation processes, clinical translation challenges, interdisciplinary cooperation, international exchange, relevant regulations and ethical guidelines. Overall, this review highlights the substantial potential of

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nanomaterials in oncology treatment, emphasizing the need for careful consideration of safety concerns to ensure their safe and effective application. The authors conclude that strengthening interdisciplinary cooperation and international exchange will contribute to the healthy development of nanomaterials in oncology treatment.

#### KEYWORDS

Tumour therapy; Nanomaterials; Interdisciplinary cooperation; Oncology treatment

#### **1. Introduction**

Oncology treatment has consistently faced substantial challenges and demands. First, early tumor diagnosis is crucial; however, many tumors are detected at intermediate or advanced stages, complicating treatment. Second, the biological heterogeneity of tumors results in diverse treatment requirements and patient responses, necessitating personalized treatment plans. Furthermore, conventional treatments, such as surgery, chemotherapy, and radiotherapy, exhibit limitations, including restricted efficacy, side effects, and toxicity issues<sup>1</sup>. Multidrug resistance is another prevalent obstacle in oncology treatment, hindering drug effectiveness. Advancements in technology have given rise to innovative therapeutic approaches like targeted therapy, immunotherapy, and gene therapy, but these still confront challenges in clinical application<sup>2</sup>. To enhance oncology treatment efficacy, researchers are dedicated to discovering novel materials and technologies. Nanomaterials possess unique physical and chemical properties, such as a high surface area-to-volume ratio, surface modifiability, and size control, rendering them suitable for numerous medical applications<sup>3</sup>. In drug delivery, nanoscale drug delivery systems offer new possibilities for oncology treatment by augmenting drug bioavailability, mitigating toxicity, improving targeting, and overcoming drug resistance<sup>4</sup>. Additionally, nanotechnology can be employed to develop controlled-release drugs, reducing side effects and bolstering efficacy<sup>5</sup>. In immunotherapy, nano-vaccines and nano-immunomodulators show promise in enhancing patients' immune responses and optimizing tumor treatment<sup>6,7</sup>. Nanotechnology applications in photothermal therapy, photodynamic therapy, radiotherapy, and nuclear medicine have further broadened oncology treatment methods<sup>8</sup>. In the realm of tumor diagnosis and imaging, nano-biomarkers and nanoprobes have advanced early tumor detection and imaging quality<sup>9</sup>. Nanotechnology also facilitates precise diagnosis and treatment of tumors while supporting individualized therapy<sup>10</sup>. Despite accomplishments in medicine, nanotechnology warrants attention regarding safety, biocompatibility, regulatory, and ethical concerns to ensure its effectiveness and safety in clinical applications. Continued research and development of nanotechnology promise to deliver more innovative applications and treatments to the medical field. This review will offer an overview of basic concepts, research processes, recent advancements, and potential future trends in the aforementioned topics, aiming to inform relevant research.

#### 2. Basic concepts of nanomaterials

Nanomaterials are materials with dimensions within the 1-100 nanometer range. These materials exhibit distinct physical, chemical, and biological properties compared to micronsized or macroscopic materials, owing to their unique dimensions. The large surface area-tovolume ratio of nanomaterials enables a wide array of applications across optics, electronics, magnetism, catalysis, and biomedicine<sup>11</sup>.

Nanomaterials can be broadly classified into the following categories based on their structural characteristics (Figure 1): (1) Nanoparticles: Nanoparticles are solid particles with nanometer dimensions. They can be inorganic (e.g., gold, silver, oxides) or organic (e.g., polymers, liposomes). Applications for nanoparticles include drug delivery, photothermal therapy, and photodynamic therapy<sup>12.</sup> (2) Nanofibers: Nanofibers are thread-like materials **Cancer Insight | 2023 2(2) 1-21** 3

featuring nanoscale diameters. Examples encompass carbon nanotubes, inorganic nanowires, and polymer nanofibers. Due to their high strength, elasticity, and electrical conductivity, nanofibers have extensive applications in sensors, catalysts, and biomedicine<sup>13</sup>. (3) Nanofilms: Nanofilms are two-dimensional materials with nanometer-scale thicknesses, such as graphene and molybdenum disulfide. Possessing unique optical, electronic, and mechanical properties, nanofilms are utilized in optoelectronic devices, energy storage, and biomedical applications<sup>14</sup>. (4) Nanoporous materials: Nanoporous materials contain nanoscale pores, exemplified by mesoporous silicon and metal-organic frameworks (MOFs). Owing to their high specific surface area and easily accessible pores for the storage and transport of small molecules, nanoporous materials: Nano-biomaterials are nanoscale materials derived or synthesized from living organisms, such as proteins, nucleic acids, and viruses. With extensive applications in biomedical fields, nano-biomaterials are used for drug delivery, gene therapy, and tissue engineering<sup>16</sup>. In the subsequent sections, we will provide an overview of nanomaterials based on their respective application areas (Figure 2).

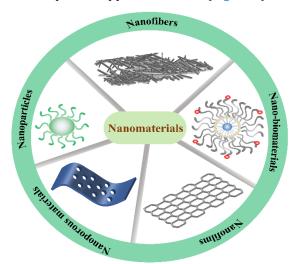
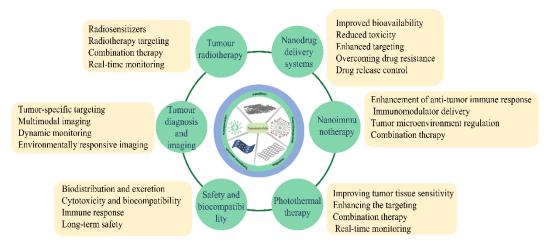


Figure 1. The main classification of nanomaterials



**Figure 2.** Application and characteristics of nanomaterials in tumor treatment **3.** Nanodrug delivery systems in oncology therapy

Nanodrug delivery systems (NDDS) have significant applications in oncology therapy. By encapsulating drugs within nanocarriers, NDDS can enhance drug bioavailability, reduce toxicity, improve targeting, and overcome drug resistance, thereby boosting the efficacy of oncology treatment (Figure 3). (1) Improved bioavailability: Conventional chemotherapeutic drugs are widely distributed throughout the body, often leading to insufficient drug concentrations in tumor tissue for adequate therapeutic effects. NDDS can increase drug concentrations in tumor tissue, thereby improving bioavailability. For instance, using polymeric or lipid nanoparticles as carriers can enhance the solubility of poorly water-soluble drugs and increase their stability in the body<sup>17</sup>. (2) Reduced toxicity: The non-specific distribution of chemotherapeutic drugs in the body can cause damage to healthy tissues, resulting in serious toxic side effects. NDDS can minimize drug impact on normal tissues and reduce toxicity. The nanocarrier surface can be modified with targeting molecules, allowing the drug to accurately identify and selectively act on tumor cells, minimizing damage to normal tissues<sup>18</sup>. (3) Enhanced targeting: NDDS can leverage the characteristics of the tumor microenvironment to achieve both active and passive targeting. Passive targeting primarily relies on the enhanced permeability and retention (EPR) effect of tumor tissue, enabling nanocarriers to accumulate in tumor tissue. Active targeting, conversely, attains specific recognition and binding to tumor cells by modifying tumor-specific molecules (e.g., antibodies, ligands) on the nanocarrier surface. By enhancing targeting, NDDS can increase drug concentrations in tumor tissues, thus improving efficacy<sup>19.</sup> (4) Overcoming drug resistance: Tumor cell resistance to chemotherapeutic drugs is a crucial factor affecting therapeutic outcomes. NDDS can potentially overcome tumor drug resistance through various mechanisms, such as altering drug action routes, bypassing drug resistance pumps, and combining multiple drugs. For example, nanocarriers can protect drugs from degradation by extracellular enzymes, thus enhancing drug stability; nanocarriers enter tumor cells via the endoplasmic reticulum pathway, bypassing the drug efflux pump and mitigating the impact of multidrug resistance; additionally, packaging multiple drugs in the same nanocarrier can enable combination therapy and decrease the risk of drug resistance<sup>20</sup>. (5) Drug release control: NDDS can achieve both sustained and triggered drug release. By designing responsive nanocarriers, drugs can be released under specific physiological conditions, such as acidic tumor microenvironments, redox environments, or light exposure. This helps to lower drug concentrations in normal tissues, reduce toxic side effects, and enhance the safety and efficacy of tumor treatment<sup>21</sup>. (6) Combination therapy: Nanodrug delivery systems can enable the combination of multiple therapies, such as chemotherapy, immunotherapy, gene therapy, photothermal therapy, and photodynamic therapy. By packaging drugs or functional molecules from different therapies in the same nanocarrier, synergistic effects can be attained to improve the effectiveness of tumor treatment. For instance, nanocarriers can carry both chemotherapeutic drugs and immunomodulators to enhance apoptosis and immune responses of tumor cells through combined action<sup>22</sup>.

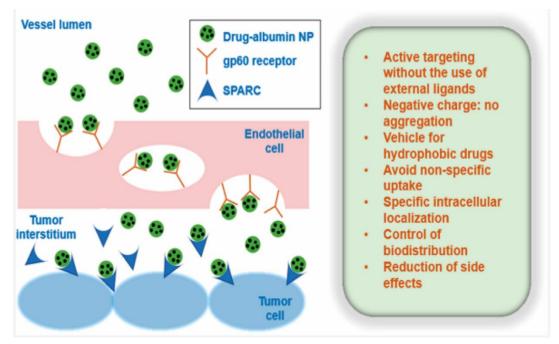


Figure 3. Application principle of nanodrug delivery system in tumor therapy

#### 4. Nanoimmunotherapy in tumour treatment

The application of Nanoimmunotherapy in oncology treatment primarily involves using nanotechnology to enhance the effectiveness of tumor immunotherapy (Figure 4). Tumor immunotherapy aims to recognize and eliminate tumor cells by activating or modulating the patient's immune system. Nanoimmunotherapy can improve the targeting of immunotherapy, reduce side effects, and enable multimodal treatment. The following are some applications of Nanoimmunotherapy in tumor therapy: (1) Enhancement of anti-tumor immune response: Nanoimmunotherapy can enhance the body's anti-tumor immune response by carrying immunostimulants or immunomodulators. For instance, using nanocarriers to package tumor antigens and immune adjuvants can enhance tumor-specific immune responses by improving antigen delivery efficiency and stimulating the activation of antigen-presenting  $cells^{23}$ . (2) Immunomodulator delivery: Nanoimmunotherapy can achieve effective delivery of immunomodulators, including immune checkpoint inhibitors such as anti-CTLA-4, anti-PD-1, and anti-PD-L1. Through the application of nanocarriers, the targeting of immunomodulators can be improved, and systemic toxicity and side effects can be reduced<sup>24</sup>. (3) Tumor microenvironment regulation: Nanoimmunotherapy can improve the infiltration and function of immune cells by regulating the tumor microenvironment. For example, using nanocarriers to deliver acidity regulators or redox regulators can alter the acidity or redox status of the tumor microenvironment and improve the activity of immune cells<sup>25</sup>. (4) Combination therapy: Nanoimmunotherapy can achieve the combination of multiple therapeutic methods, such as immunotherapy with chemotherapy, photothermal therapy, or gene therapy. Nanocarriers can carry multiple drugs or functional molecules simultaneously to achieve combined effects and improve apoptosis and immune response of tumor cells<sup>26</sup>. (5) Immunodiagnosis and efficacy monitoring: Nanoimmunotherapy can be applied to tumor

immunodiagnosis and efficacy monitoring. Nanomaterials have excellent optical, magnetic, and electrical properties and can be used as tumor markers for detection and imaging. For instance, nanoparticles can bind to tumor-associated antigens or immune cells to enable early diagnosis of tumors and monitoring of the disease course<sup>27</sup>. In addition, nanocarriers can be used to monitor the efficacy of immunotherapy, e.g., to assess the infiltration and activity of immune cells in tumor tissue<sup>28</sup>. (6) Vaccine delivery: Nanoimmunotherapy can also be used for the delivery of tumor vaccines. Tumor vaccines are a therapeutic approach that uses tumor antigens to activate the body's immune system. Nanocarriers can effectively deliver tumor antigens and immune adjuvants to enhance the immune response to the vaccine. For example, nanoparticles can package tumor antigenic peptides or tumor cell lysates to enhance the delivery efficiency and immunogenicity of tumor antigens<sup>29</sup>. (7) Combination of gene editing technologies: Nanoimmunotherapy can be combined with gene editing technologies to achieve modification of immune cell function. For example, using gene editing tools such as CRISPR/Cas9 delivered by nanocarriers can achieve targeted modification of T-cell receptors (TCR) or chimeric antigen receptors (CAR) to improve the recognition and killing ability of immune cells against tumor cells<sup>30</sup>.

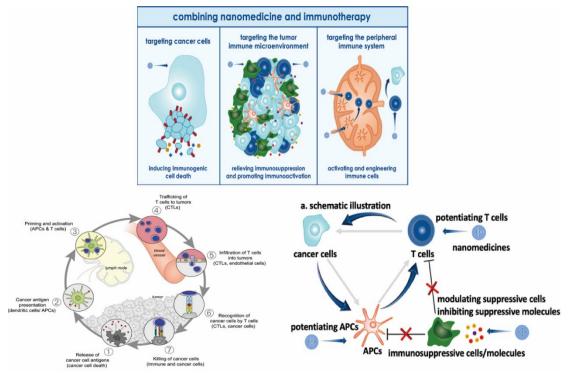


Figure 4. Principle of nanoimmunotherapy in tumor treatment

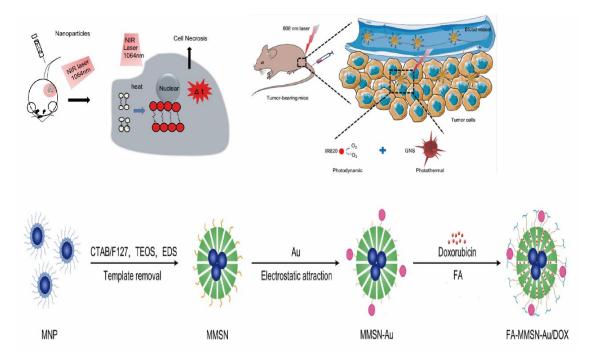
# 5. Nanomaterials in tumour photothermal therapy and photodynamic therapy

The application of nanomaterials in tumor photothermal therapy and photodynamic therapy holds significant potential (<u>Figure 5</u>). Photothermal therapy uses light-sensitive nanomaterials to convert light energy into heat energy, producing a localized heating effect on tumor cells, leading to apoptosis. Photodynamic therapy uses light-sensitive nanomaterials to

generate highly reactive oxidative effects on tumor cells by producing singlet oxygen in the activated state under light illumination, causing tumor cell death. The applications of nanomaterials in tumor photothermal therapy and photodynamic therapy are described below, respectively.

The application of nanomaterials in tumor photothermal therapy includes the following aspects: (1) Improving tumor tissue sensitivity to photothermal effects: nanomaterials have excellent light absorption properties and can efficiently convert light energy into heat energy. This efficient photothermal conversion property makes nanomaterials highly valuable in photothermal therapy<sup>31</sup>. (2) Enhancing the targeting of photothermal therapy: By modifying targeting molecules on the surface, nanomaterials can achieve targeted aggregation in tumor tissues, improving the local therapeutic effect of photothermal therapy and reducing damage to healthy tissues<sup>32</sup>. (3) Combination therapy: Nanomaterials can be combined with other therapeutic methods such as chemotherapy drugs or immunotherapy to achieve combination therapy. The heating effect of photothermal therapy can enhance drug release and penetration, and improve cell sensitivity to drugs, thus enhancing the therapeutic effect<sup>33</sup>. (4) Real-time monitoring: The application of nanomaterials in photothermal therapy can also enable realtime temperature monitoring. For example, metallic nanomaterials can provide real-time feedback of temperature information through spectral signals, which helps monitor temperature changes during the treatment process and ensure treatment effectiveness and safety<sup>34.</sup>

The applications of nanomaterials in tumor photodynamic therapy include the following: (1) Improving the bioavailability of photosensitizers: Nanomaterials can encapsulate photosensitizers or modify their surface to improve their bioavailability. Nanocarriers can protect photosensitizers from intrabody degradation and improve their stability and biocompatibility<sup>35</sup>. (2) Enhancing the targeting of photodynamic therapy: Nanocarriers can achieve specific recognition and aggregation in tumor tissue by surface modification of tumorspecific targeting molecules, such as antibodies, peptides, and receptor ligands. This helps enhance the targeting of photodynamic therapy and reduce damage to normal tissues<sup>36</sup>. (3) Combination therapy: Nanomaterials in photodynamic therapy can be combined with other therapeutic tools to achieve combination therapy. For example, combining photosensitizers with chemotherapeutic drugs or immunotherapy can achieve apoptosis of tumor cells under photodynamic therapy action while enhancing the effect of other therapeutic tools<sup>37</sup>. (4) Photodynamic therapy diagnosis and monitoring: Nanomaterials can be used as fluorescent probes to achieve real-time monitoring during tumor diagnosis and treatment. For example, co-loading fluorescent probes with photosensitizers in nanocarriers can enable fluorescence imaging of tumor tissues, guiding the treatment process of photodynamic therapy<sup>38</sup>. (5) Overcoming limitations in photodynamic therapy: Nanomaterials can overcome some limitations in photodynamic therapy, such as poor light penetration and low selectivity of photosensitizers. Nanomaterials can achieve deeper treatment of tumor tissues by changing the absorption wavelength of photosensitizers. Simultaneously, nanocarriers can improve the selectivity of photosensitizers and reduce damage to normal tissues<sup>39</sup>.



**Figure 5.** The operating principle of nanomaterials in tumor photothermal therapy and photodynamic therapy

#### 6. Nanomaterials in tumour radiotherapy and nuclear medicine

The use of nanomaterials in radiotherapy and nuclear medicine for oncology has a wide range of promising applications to improve treatment effectiveness, reduce side effects, enable multimodal treatment, and facilitate early diagnosis of tumors and monitoring of the treatment process. We illustrate examples of nanomaterials in radiotherapy (Figure 6A) and nuclear medicine applications (Figure 6B) separately.

The applications of nanomaterials in tumor radiotherapy are mainly as follows: (1) Radiosensitizers: nanomaterials can be used as radiosensitizers to improve the sensitivity of tumor cells to radiotherapy. For example, gold nanoparticles have an excellent dose enhancement effect in radiotherapy, which can increase the local deposition of radiation dose in tumor tissues and improve the apoptosis rate of tumor cells<sup>40</sup>. (2) Radiotherapy targeting: nanomaterials can achieve targeted aggregation in tumor tissue through surface modification of specific targeting molecules, improving the local therapeutic effect of radiotherapy and reducing damage to normal tissue<sup>41</sup>. (3) Combination therapy: Nanomaterials can be combined with other therapeutic methods in radiotherapy to achieve combination therapy. For example, combining radiotherapy with chemotherapy, photothermal therapy, and photodynamic therapy can improve the therapeutic effect and reduce side effects<sup>42</sup>. (4) Real-time monitoring: The application of nanomaterials in radiotherapy can also enable real-time monitoring during the treatment process. For example, nanomaterials can be used as fluorescent probes to achieve real-time imaging during tumor diagnosis and treatment, which can help guide the radiotherapy treatment process<sup>43</sup>.

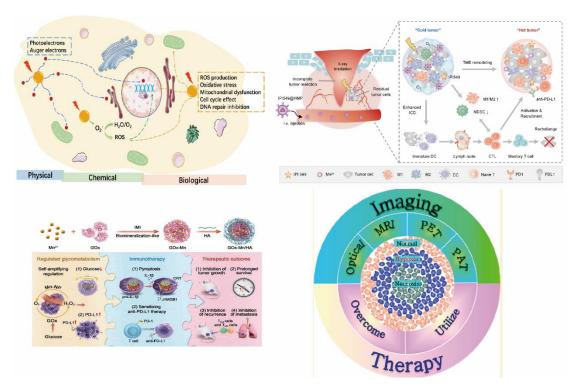


Figure 6A. The workflow of Nanomaterials in tumour radiotherapy

The applications of nanomaterials in nuclear medicine are mainly as follows: (1) Nucleotide targeting therapy: nanomaterials can be used as carriers of nucleotides to achieve targeted delivery of nucleotides and improve the effectiveness of nuclear medicine therapy. For example, nanoparticles can be surface-modified with tumor-specific targeting molecules to achieve specific recognition and aggregation in tumor tissue and reduce damage to normal tissue<sup>44</sup>. (2) Nuclide diagnosis: Nanomaterials can be used as carriers of nuclides to achieve early diagnosis and disease monitoring of tumors. For example, nanoparticles can be surfacemodified with radionuclides, such as technetium-99 and fluorine-18, to achieve specific recognition and imaging of tumor tissues. These radionuclides can be combined with imaging techniques such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) to improve the accuracy and sensitivity of tumor diagnosis<sup>45</sup>. (3) Combined diagnosis and treatment: Nanomaterials in nuclear medicine can achieve a combination of diagnosis and treatment. For example, by co-loading radionuclides with drugs or other therapeutic methods in nanocarriers, the same nanoparticles can be used for both diagnostic and therapeutic functions. This combined treatment strategy can help improve the precision of tumor treatment and reduce side effects<sup>46</sup>. (4) Radioprotective agents: Nanomaterials can also be used as radioprotective agents to reduce the damage to normal tissues from radiation therapy. For example, some nanomaterials have strong free radical scavenging ability, which can reduce the oxidative damage to normal tissues caused by radionuclides<sup>47</sup>. (5) Personalized treatment: The application of nanomaterials in nuclear medicine can enable personalized treatment. By selecting different nanocarriers, nuclides, and targeting molecules, personalized treatment plans can be developed for various types and molecular subtypes of tumors to improve the therapeutic effect<sup>48</sup>.

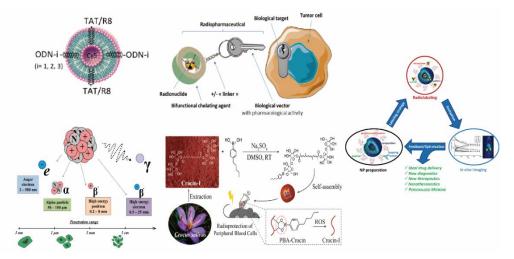


Figure 6B. The workflow of Nanomaterials in nuclear medicine

#### 7. Nanomaterials in tumour diagnosis and imaging

Nanomaterials have a wide range of promising applications in tumor diagnosis and imaging, which can improve the accuracy, sensitivity, and specificity of tumor diagnosis and enable early detection, early diagnosis, and real-time monitoring of the treatment process (Figure 7). The following are some of the major applications of nanomaterials in tumor diagnosis and imaging: (1) Tumor-specific targeting: Nanomaterials can achieve specific recognition and aggregation in tumor tissue through surface modification of tumor-specific targeting molecules, such as antibodies, peptides, and receptor ligands. This helps to improve the specificity of tumor diagnostic imaging and reduce the false-positive rate<sup>49</sup>. (2) Multimodal imaging: Nanomaterials can be used as multimodal imaging probes, enabling the combination of multiple imaging techniques to improve the accuracy and sensitivity of tumor diagnosis. For example, nanomaterials can be used as probes for multiple imaging modalities such as magnetic resonance imaging (MRI), positron emission tomography (PET), singlephoton emission computed tomography (SPECT), and optical imaging at the same time, achieving complementary and integrated multimodal imaging<sup>50</sup>. (3) Dynamic monitoring: The application of nanomaterials in tumor diagnosis can also enable dynamic monitoring during the treatment process. For example, the use of nanomaterials as fluorescent probes can enable real-time imaging of tumor tissue, which can help guide the treatment process and assess treatment effects<sup>51</sup>. (4) Environmentally responsive imaging: Nanomaterials can be designed as environmentally responsive imaging probes to achieve specific imaging of the tumor microenvironment. For example, using nanomaterials to identify and image acidity, hypoxia, or specific enzymes in the tumor microenvironment can help reveal the biological characteristics and pathological processes of tumors<sup>52</sup>. (5) Molecular typing diagnosis: The application of nanomaterials in tumor diagnosis can also enable the diagnosis of molecular subtypes of tumors. By selecting different target molecules and imaging methods, personalized diagnosis and typing can be achieved for different types and molecular subtypes of tumors<sup>53</sup>. (6) Biomarker detection: Nanomaterials can be applied to the detection of tumor biomarkers, for example, by using nanoparticles to enhance the signal intensity and improve

the sensitivity and accuracy of biomarker detection. In addition, nanomaterials can be used for the detection of liquid biopsies such as circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA), which can help to achieve early diagnosis and disease course monitoring<sup>54.</sup> (7) Development of novel imaging techniques using nanomaterials: The application of nanomaterials in the field of tumor diagnosis can also facilitate the development of novel imaging techniques. For example, nanoparticles can be used as photoacoustic imaging probes to achieve high-resolution and high-contrast imaging of tumor tissue<sup>55.</sup>

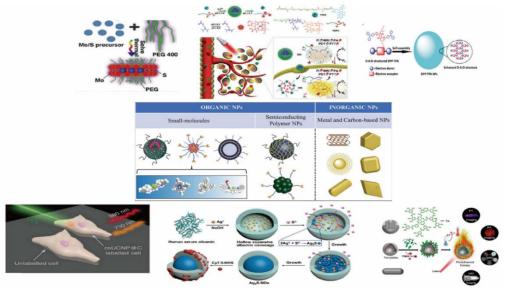


Figure 7. The application principles of nanomaterials in tumor diagnosis and imaging

#### 8. Safety and biocompatibility issues of nanomaterials in tumour therapy

Nanomaterials have great potential in oncology therapy, but in practical applications, safety and biocompatibility issues are challenges that cannot be ignored. The following are the main aspects of safety and biocompatibility issues for nanomaterials in oncology therapy: (1) Biodistribution and excretion: The biodistribution and excretion of nanomaterials in the body are important factors affecting their safety and biocompatibility. Ideally, nanomaterials should have a good biodistribution in the body, be able to reach the target tissue quickly, and be excreted rapidly after treatment. However, the aggregation and prolonged retention of some nanomaterials in the body can lead to potential toxicity and side effects. Therefore, when designing nanomaterials, their biodistribution and excretion properties need to be fully considered to reduce the impact on normal tissues<sup>56</sup>. (2) Cytotoxicity and biocompatibility: Nanomaterials may cause toxicity to cells, such as oxidative stress, inflammatory response, genotoxicity, etc. In addition, the surface properties, shape, size, and other factors of nanomaterials may also affect their biocompatibility. When developing new nanomaterials, systematic evaluation of their cytotoxicity and biocompatibility is needed to optimize the design and preparation process of nanomaterials to reduce their potential toxicity and side effects<sup>57</sup>. (3) Immune response: Nanomaterials may trigger immune responses in vivo, such as inflammatory reactions and allergic reactions. When designing nanomaterials, their immunocompatibility should be considered to avoid triggering undesirable immune

responses. In addition, the immunogenicity of nanomaterials can be reduced and their biocompatibility improved through strategies such as surface modification and carrier selection<sup>58</sup>. (4) Long-term safety of nanomaterials: The long-term safety of nanomaterials in vivo is unclear. Some nanomaterials may accumulate in vivo, leading to potential long-term toxicity. Therefore, long-term safety assessment and monitoring are needed in the clinical application of nanomaterials<sup>59</sup>. (5) Individual differences: The safety and biocompatibility of nanomaterials may vary among individuals. In clinical applications, individualized treatment plans need to be developed according to individual patient differences to reduce the risk of potential toxicity and side effects. In addition, large-scale clinical trials are needed to assess the safety and biocompatibility of nanomaterials in different patient groups $^{60}$ . (6) Quality control of nanomaterials: Due to the complex preparation process of nanomaterials, quality control has an important impact on their safety and biocompatibility (Figure 8). During the production of nanomaterials, a strict quality control system needs to be established to ensure the quality stability and consistency of nanomaterials and to reduce potential safety risks<sup>61</sup>. (7) Scale production and clinical transformation of nanomaterials: The scale production and clinical transformation of nanomaterials is the key to their widespread application. During the development of nanomaterials, challenges in the preparation process, quality control, and cost need to be overcome to ensure that the safety and biocompatibility of nanomaterials are fully guaranteed<sup>62</sup>. (8) Regulatory policies and ethical issues: As the application of nanomaterials in tumor therapy gradually advances, regulatory policies and ethical issues are also becoming increasingly prominent. Governments and regulatory agencies need to develop appropriate policies and guidelines to ensure that the clinical application of nanomaterials complies with safety, efficacy, and ethical principles. In addition, medical teams, researchers, and patients also need to work together to promote the safe, effective, and sustainable development of nanomaterials in oncology treatment<sup>63</sup>.

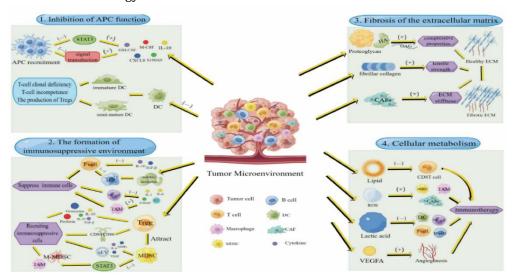


Figure 8. The main aspects of safety and biocompatibility of nanomaterials in tumor treatment

#### 9. Nanomaterials in individualized tumour therapy

Individualised oncology treatment refers to the development of personalised treatment plans based on information about a patient's genes, protein expression and biomarkers in order to improve treatment efficacy and reduce side effects (Figure 9). The application of nanomaterials in individualised oncology therapy has great potential, and the following are some of the key aspects: (1) Targeted drug delivery: Nanodrug delivery systems can selectively deliver drugs to tumour tissue based on patient-specific surface markers of tumour cells, reducing the distribution of drugs in normal tissue, thereby reducing side effects and improving treatment efficacy. Through surface modification and carrier selection, nano drug delivery systems can be optimised for individual patient differences<sup>64</sup>. (2) Multimodal therapy: Nanomaterials can enable the combination of multiple therapeutic modalities, such as integrating drugs, photothermal therapy and photodynamic therapy into a single nanoparticle, to achieve combined therapy and improve therapeutic efficacy. According to the biological characteristics and clinical needs of the patient's tumour, a personalised multimodal treatment plan can be developed<sup>65</sup>. (3) Treatment monitoring and adjustment: The application of nanomaterials in tumour diagnosis and imaging can help monitor the treatment process in real time and provide a basis for the adjustment of treatment plans. For example, nanoparticles can be used in photoacoustic imaging to monitor the process of tumour growth, shrinkage and blood vessel formation in real time, providing clinicians with important information that can help to develop individualised treatment plans<sup>66</sup>. (4) Nanoimmunotherapy: Nano-immunotherapy can be used to design personalised treatment strategies that target the immune phenotype of a patient's tumour cells. For example, nanoparticles can be used to deliver tumour antigens and immunostimulants to induce the patient's own immune system to attack the tumour cells, enabling individualised immunotherapy<sup>67.</sup> (5) Gene therapy: Nanomaterials can be used as carriers for gene therapy, delivering genes with therapeutic potential to tumour cells. Depending on the gene mutation and expression abnormality of the patient's tumour, targeted genes can be selected for treatment. For example, nanoparticles are used to deliver short interfering RNA (siRNA) or CRISPR/Cas9 systems to target specific tumour-related genes for editing and individualised gene therapy<sup>68</sup>. (6) Drug screening and quantitative individualised drug delivery: Nanomaterials can be used to screen the sensitivity of a patient's tumour to different drugs and thus optimise individualised treatment regimens. In addition, nanodrug delivery systems can be used to dose and release loads of drugs to achieve quantitative individualised drug delivery to meet the specific therapeutic needs of patients<sup>69</sup>. (7) Individualised tumour vaccines: Nanomaterials can be applied to the development of individualised tumour vaccines. By extracting specific antigens from the patient's tumour tissue, combined with appropriate immunostimulants and nanocarriers, individualised tumour vaccines can be prepared to activate the patient's own immune system to attack the tumour<sup>70.</sup> (8) Drug combination optimisation: Nanomaterials can achieve synergistic treatment of multiple drugs to improve the therapeutic effect. According to the biological characteristics and clinical needs of the patient's tumour, a personalised drug combination can be developed to optimise the therapeutic effect<sup>71.</sup>.

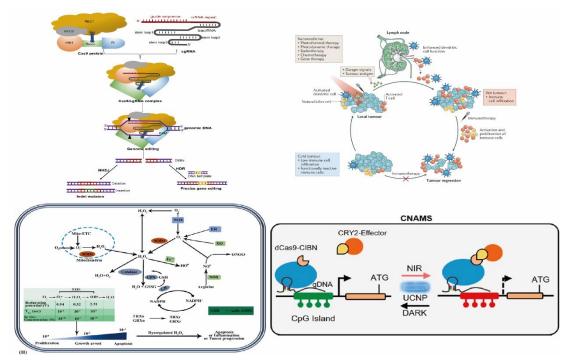


Figure 9. The application of nanomaterials in individualised oncology therapy

#### 10. Future trends and challenges

With the continuous development of nanotechnology, the application of nanomaterials in tumor treatment is also expanding. Future development trends and challenges include the following: (1) Development of multi-functional integrated nanomaterials: In order to improve treatment effects and reduce side effects, more multi-functional integrated nanomaterials will emerge in the future, such as the integration of diagnostic, therapeutic, and monitoring functions in a single nanoparticle. The development of such multi-functional integrated nanomaterials will help to achieve precise control and individual adjustment of tumor treatment<sup>72, 73</sup>. (2) Development of smart nanomaterials: Smart nanomaterials can undergo reversible or irreversible changes in shape, structure, and function according to environmental conditions (e.g., pH, temperature, enzyme activity, etc.) to achieve targeted release of drugs and improved therapeutic effects. In the future, the application of smart nanomaterials in tumor therapy will receive more extensive attention and research<sup>7</sup>. (3) Research on nano-biomaterials: With good biocompatibility and biodegradability, nanobiomaterials can be used in drug delivery and immunotherapy for tumor treatment. As research on nano-biomaterials continues to progress, their application in tumor therapy will receive more attention<sup>74</sup>. (4) Deepening of individualized tumor therapy: In the future, the application of nanomaterials in individualized tumor therapy will be further developed. Through in-depth analysis of the genome, proteome, and metabolome information of patients' tumors, nanomaterials will provide patients with more accurate and personalized treatment plans<sup>75.</sup> (5) Integration of nanotechnology with other technologies: The integration of nanotechnology with cutting-edge technologies such as gene editing and cell therapy will bring new breakthroughs in tumor treatment. Through nanotechnology, these cutting-edge technologies can be better realized and applied, bringing more possibilities for tumor treatment<sup>76, 77.</sup>

However, there are still some challenges in the application of nanomaterials in oncology

treatment: (1) Safety and biocompatibility: The biodistribution, metabolism, and excretion processes of nanomaterials in the body may affect their safety and biocompatibility. Studies on the long-term toxicity and immunogenicity of nanomaterials are still inadequate and need to be further explored to ensure their safety in clinical applications. (2) Preparation process and quality control: The preparation process and quality control of nanomaterials have an important impact on their application in oncology treatment. More efficient and controllable preparation methods need to be developed in the future to improve the stability, bioactivity, and drug loading of nanomaterials. (3) Clinical translation: Although nanomaterials have achieved many results in laboratory research, their promotion in clinical applications still faces many challenges. Clinical trials of nanomaterials in tumor therapy need to be strengthened to verify their efficacy, safety, and feasibility. (4) Interaction between nanomaterials and tumor microenvironment: The tumor microenvironment has an important influence on the therapeutic effects of nanomaterials. The interaction mechanism between nanomaterials and the tumor microenvironment needs to be studied in-depth in the future to improve the targeting and efficacy of nanomaterials in tumor therapy. (5) Interdisciplinary research and cooperation: The application of nanomaterials in tumor therapy involves multiple disciplines, such as materials science, biology, and medicine. Strengthening interdisciplinary research and cooperation will help to promote more breakthroughs in the application of nanomaterials in tumor therapy. (6) Regulatory and ethical issues: The application of nanomaterials in oncology treatment involves a number of regulatory and ethical issues, such as patient privacy protection and informed consent. The development of appropriate regulations and ethical guidelines can help ensure that the application of nanomaterials in oncology treatment is reasonably regulated.

In conclusion, nanomaterials have significant potential and development prospects in tumor therapy. As nanotechnology continues to advance and interdisciplinary research progresses, more breakthroughs in the application of nanomaterials in tumor therapy will be achieved. However, several challenges must be addressed, including biosafety, biocompatibility, preparation processes, and clinical translation, to ensure the safe and effective application of nanomaterials in tumor therapy. Strengthening interdisciplinary cooperation and international exchange, as well as promoting the improvement of relevant regulations and ethical guidelines, will contribute to the healthy development of nanomaterials in oncology treatment. By addressing these challenges, we can harness the advantages of nanomaterials in tumor treatment and provide patients with more precise and personalized treatment plans. Furthermore, we should focus on integrating nanotechnology with other cutting-edge technologies and explore the application of nanotechnology in areas such as gene editing and cell therapy to bring new breakthroughs in tumor treatment. Finally, emphasizing the education and popularization of nanotechnology in tumor treatment and increasing public awareness and acceptance of nanotechnology will also help the widespread application of nanomaterials in the field of tumor treatment. With the further development of nanotechnology in tumor treatment, we expect nanomaterials to bring hope and good news to more tumor patients.

#### **Conflict of interest**

All the authors claim that the manuscript is completely original. The authors also declare no conflict of interest.

Author contributions Cancer Insight | 2023 2(2) 1-21 Conceptualization: Hongmei Yang, Qiang Xie; Investigation: Chen Li, Qiang Xie; Methodology: Qiang Xie; Writing–original draft: Hongmei Yang; Writing–review & editing: Hongmei Yang, Qiang Xie.

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