

Review Article

Nanomaterials in Medicine: Advancing Drug Delivery, Diagnostics, and Therapeutics

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Abstract: Nanomaterials have revolutionized various fields of medicine, providing innovative solutions for drug delivery, diagnostics, vaccines, and regenerative therapies. The aim of this review is to explore the diverse applications of nanomaterials in medicine, highlighting their potential to enhance treatment efficacy, improve patient outcomes, and address complex medical challenges. Through successful applications like Doxil and Abraxane, nanotechnology has demonstrated its ability to improve targeted drug delivery, while lipid nanoparticles have played a pivotal role in the development of mRNA vaccines for COVID-19. Nanomaterials offer unique advantages, such as their small size, tunable surface properties, and the ability to cross biological barriers, which enable precision therapies and improved diagnostic sensitivity. However, this review also addresses the challenges associated with nanomaterials, including safety concerns, potential toxicity, long-term biodegradability, and the regulatory hurdles that must be overcome for clinical translation. As researchers work to develop biocompatible and biodegradable materials, new opportunities arise in personalized medicine, stimuli-responsive nanomaterials, and theranostics that combine diagnosis and therapy into a single platform. In conclusion, while nanotechnology in medicine offers immense potential for future medical innovations, addressing safety and regulatory challenges will be crucial for the broader adoption of nanomaterials in clinical practice. This review emphasizes the need for continued research and development to realize the full potential of nanomedicine in improving healthcare outcomes globally.

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1. INTRODUCTION

In recent decades, the rapid advancements in nanotechnology have ushered in a new era of innovation, profoundly impacting numerous scientific disciplines. One of the most promising fields to benefit from these developments is medicine, where nanomaterials are redefining the ways diseases are diagnosed, treated, and even prevented (W. Lu et al., 2021). Nanomaterials, substances engineered at the nanoscale, typically less than 100 nanometers in size, exhibit unique physical, chemical, and biological properties that distinguish them from their bulk counterparts. These characteristics, such as enhanced surface area, tunable optical and electrical properties, and the ability to interact with biological systems at the molecular level, make nanomaterials ideal candidates for medical applications (J. K. Patel et al., 2021).

The integration of nanomaterials into medicine and drug production has already begun to transform traditional approaches, leading to the development of more efficient drug delivery systems, innovative diagnostic tools, and novel therapeutic strategies. For example, nanoparticles can be engineered to deliver drugs with unprecedented precision, targeting specific tissues or cells while minimizing side effects, a capability particularly useful in cancer therapy (Ahmad et al., 2019). Similarly, nanoscale materials are being harnessed in medical imaging and biosensors, offering improved sensitivity and accuracy in disease detection (Welch et al., 2021).

Despite the tremendous potential, the use of nanomaterials in medicine also presents challenges, including issues related to toxicity, biocompatibility, and regulatory approval (Xuan et al., 2023). Nevertheless, ongoing research and clinical trials continue to reveal the extraordinary potential of these materials to revolutionize healthcare and pharmaceutical development. This review explores the diverse applications of nanomaterials in medicine and drug production, emphasizing their role in drug delivery, diagnostics, therapeutics, and vaccine development, while also addressing the challenges and future directions in this evolving field.

2. NANOPARTICLES

Nanoparticles are some of the most versatile nanomaterials in medicine, with a broad range of applications due to their ability to be engineered for specific functions such as drug delivery, imaging, and diagnostics. Their size, shape, and surface properties can be tuned to achieve optimal performance in various biomedical applications.

2.1. Metallic Nanoparticles

Metallic Nanoparticles such as gold, silver, and iron oxide nanoparticles offer significant potential in both therapeutic and diagnostic applications. Gold nanoparticles (AuNPs) are highly biocompatible and easily functionalized with biomolecules like antibodies or drugs, making them ideal for targeted therapies and photothermal therapy, where they convert near-infrared light into heat to destroy cancer cells (Dheyab et al., 2023). Beyond therapy, AuNPs are also extensively used in diagnostics, particularly in biosensors and imaging (Oliveira et al., 2023). Silver nanoparticles (AgNPs) are renowned for their potent antimicrobial properties, exhibiting strong antibacterial, antiviral, and antifungal activities (Almatroudi, 2024). They are frequently used in wound dressings, medical device coatings, and antimicrobial treatments due to their ability to disrupt microbial cell membranes, generate reactive oxygen species (ROS), and release silver ions, leading to microbial death (More et al., 2023). Lastly, iron oxide nanoparticles (SPIONs), are invaluable in medical imaging, serving as contrast agents in magnetic resonance imaging (MRI) to enhance the visibility of tissues (Shen et al., 2024). Additionally, SPIONs are being researched for targeted drug delivery and hyperthermia treatments, where they generate localized heat to eliminate cancer cells under an external magnetic field (Spoială et al., 2023).

2.2. Polymeric Nanoparticles

Polymeric Nanoparticles are highly versatile in drug delivery, particularly for controlled and targeted therapies. Biodegradable

polymeric nanoparticles, made from polymers like polylactic acid (PLA), polyglycolic acid (PGA), and polylactic-co-glycolic acid (PLGA), gradually degrade in the body, making them ideal for sustained drug release (Sarkar et al., 2022). These nanoparticles protect encapsulated drugs from degradation in the bloodstream, allowing for controlled release at the target site, such as a tumor, thereby reducing systemic toxicity and side effects in cancer therapy (Madej et al., 2022). Another advanced type, stimuli-responsive nanoparticles, are designed to release their drug payloads in response to specific environmental changes such as pH, temperature, or enzymes. For instance, pH-responsive nanoparticles can release drugs in the acidic tumor microenvironment, ensuring targeted delivery to cancer cells while minimizing damage to healthy tissues (Thomas et al., 2020).

2.3. Lipid-Based Nanoparticles

Lipid-Based Nanoparticles are crucial for drug delivery systems due to their biocompatibility and ability to carry both hydrophilic and hydrophobic drugs. Solid lipid nanoparticles (SLNs), made from lipids that remain solid at body temperature, provide controlled release and high stability, making them ideal for delivering a wide range of drugs (S. Pandey et al., 2021). They are particularly useful in gene therapy, where they can encapsulate genetic material like siRNA or DNA for targeted delivery to cells (Dinh et al., 2024). An advancement over SLNs, nanostructured lipid carriers (NLCs) consist of a blend of solid and liquid lipids, which enhances their drug loading capacity and allows for more precise control over drug release (Elmowafy & Al-Sanea, 2021). NLCs are being extensively studied for delivering poorly water-soluble drugs, such as antiretroviral and anticancer agents, and have shown promise in improving the bioavailability of these medications (Haider et al., 2020; Rojekar et al., 2021).

2.4. Nanotubes and Nanofibers

Nanotubes and nanofibers are cylindrical nanomaterials that offer unique advantages for biomedical applications, particularly in drug delivery and tissue engineering due to their large surface area and hollow structure.

2.4.1. Carbon Nanotubes (CNTs)

Carbon Nanotubes (CNTs), both single-walled and multi-walled, offer unique advantages in various medical applications due to their exceptional physical and chemical properties. Single-Walled Carbon Nanotubes (SWCNTs) consist of a single layer of carbon atoms rolled into a cylinder and are known for their excellent electrical conductivity (Predtechenskiy et al., 2022). This makes them ideal for use in biosensors that detect biomarkers or monitor cellular activity. Additionally, their hollow cylindrical structure allows them to be loaded with drugs and functionalized with targeting molecules, making SWCNTs effective vehicles for delivering therapeutic agents to specific tissues or cells (Dewey et al., 2024). On the other hand, Multi-Walled Carbon Nanotubes (MWCNTs) are composed of several concentric layers of carbon atoms, providing greater robustness compared to SWCNTs (Islam et al., 2024). MWCNTs are being researched for tissue engineering and regenerative medicine, where they can act as scaffolds that promote cell growth and differentiation, aiding in the regeneration of damaged tissues (Lekshmi et al., 2020).

2.4.2. Polymer-Based Nanofibers

Polymer-Based Nanofibers, particularly electrospun and drug-eluting types, are essential tools in regenerative medicine and tissue engineering due to their structural and functional versatility. Electrospun nanofibers are created through an electrospinning process, producing fibers with diameters in the nanometer range. These nanofibers possess high porosity and surface area, characteristics that make them excellent scaffolds for tissue engineering (Y. Chen et al., 2022). They can closely mimic the extracellular matrix (ECM) of tissues, facilitating cell adhesion, proliferation, and differentiation, which are crucial for tissue regeneration (X. Zhang et al., 2022). In addition to their structural benefits, drug-eluting nanofibers can be functionalized

to release therapeutic agents in a controlled manner. This capability is especially valuable in wound healing applications, where nanofibers can deliver antibiotics, growth factors, or other drugs over time to promote accelerated tissue regeneration and prevent infections (Akombaetwa et al., 2022).

2.5. Dendrimers

Dendrimers are highly branched, tree-like polymers with well-defined structures that make them ideal candidates for precise drug delivery systems. Their multivalent surface allows for the attachment of various functional groups, including therapeutic agents, imaging molecules, and targeting ligands.

Drug Delivery Using Dendrimers offers significant advantages in terms of solubility enhancement and targeted therapy. Enhanced solubility is a key feature of dendrimers, as their internal cavities can encapsulate hydrophobic drugs, improving the solubility of compounds with otherwise poor bioavailability (Prajapati & Jain, 2020). This property is especially beneficial for the delivery of anticancer and antiviral drugs, allowing for more effective treatment (Chis et al., 2020). Additionally, targeted delivery is achieved by functionalizing the surface of dendrimers with targeting ligands, such as antibodies, peptides, or folic acid, enabling them to specifically target cancer cells. This reduces off-target effects and systemic toxicity, making the treatment safer and more efficient (Seidu et al., 2022). For example, poly(amidoamine) (PAMAM) dendrimers have been successfully used to deliver chemotherapeutic agents directly to tumor cells while minimizing damage to healthy tissues, enhancing the precision of cancer therapy (Tarach & Janaszewska, 2021).

Dendrimers can be used for theranostics, a field that combines therapy and diagnostics (Bober et al., 2022). For example, dendrimers functionalized with both drugs and imaging agents can simultaneously deliver a therapeutic agent and allow for real-time monitoring of the treatment's progress using imaging techniques such as MRI or fluorescence imaging (Ray et al., 2018).

2.6. Quantum Dots (QDs)

Quantum dots (QDs) are semiconductor nanocrystals with size-tunable optical properties, allowing precise control over their fluorescence wavelength depending on their size. This characteristic makes them highly valuable in biomedical imaging and diagnostics. In imaging applications, quantum dots offer significant advancements, particularly in cellular and molecular imaging (Wagner et al., 2019). Due to their strong fluorescence and resistance to photobleaching, quantum dots surpass traditional dyes in durability and effectiveness for long-term imaging, enabling researchers and clinicians to track biological processes in real time. This provides critical insights into disease progression and treatment efficacy (S. Huang & Huang, 2024). QDs also excel in multiplexed imaging, where they emit light at multiple wavelengths simultaneously, facilitating the visualization of several biological targets within a single sample (B. Zhang et al., 2017). This multiplexing capability is especially useful in diagnosing diseases such as cancer, where detecting multiple biomarkers is essential for an accurate and comprehensive diagnosis (Soldado et al., 2022).

Beyond imaging, QDs are being explored for their potential in drug delivery and diagnostics. QDs can be functionalized with therapeutic agents, enabling the simultaneous delivery of drugs and imaging agents (Yukawa et al., 2023). This dual-purpose approach, theranostics, offers a promising route for personalized medicine, as it allows for the monitoring and real-time adjustment of treatments based on imaging feedback. By combining diagnostic and therapeutic functionalities, quantum dots contribute to the development of highly targeted, adaptable, and patient-specific therapies, positioning them at the forefront of innovative medical applications (Abdellatif et al., 2022).

2.7. Nanocarriers

Nanocarriers, such as liposomes, micelles, and polymer-drug conjugates, are used to improve the pharmacokinetics of drugs, enhance drug stability, and enable targeted delivery.

2.7.1. Liposomes

Liposomes are versatile drug delivery systems characterized by their structure and function, consisting of phospholipid bilayers capable of encapsulating both hydrophilic and hydrophobic drugs (Nsairat et al., 2022). This encapsulation protects the drugs from degradation in the body, enhancing their stability and bioavailability (P. Liu et al., 2022). Liposomes are extensively used in cancer therapy, with liposomal formulations like Doxil® (liposomal doxorubicin) demonstrating improved efficacy and significantly reduced cardiotoxicity compared to free drugs (Lee et al., 2023). In addition to their structural advantages, targeted liposomes can be functionalized with specific targeting ligands, such as monoclonal antibodies, to direct drug delivery specifically to cancer cells (Riaz et al., 2018). This targeted approach not only minimizes off-target effects but also reduces the required dose of chemotherapy, improving therapeutic outcomes while mitigating side effects (Riaz et al., 2018).

2.7.2. Micelles

Micelles are self-assembling nanocarriers formed from amphiphilic molecules with a hydrophobic core and a hydrophilic shell, making them ideal for encapsulating hydrophobic drugs. This encapsulation enhances the solubility and stability of poorly water-soluble drugs (Bose et al., 2021). Polymeric micelles have been extensively studied for the delivery of anticancer drugs, as they preferentially accumulate in tumor tissues through the enhanced permeability and retention (EPR) effect, improving drug delivery and efficacy (Nakamura et al., 2016). Additionally, stimuli-responsive micelles are designed to release their drug payload in response to specific environmental changes, such as pH or temperature shifts (Wells et al., 2019). This controlled release mechanism further enhances the precision of drug delivery, ensuring that drugs are released at the desired site, such as in the acidic microenvironment of a tumor (Thomas et al., 2020).

3. APPLICATIONS of NANOMATERIALS in DRUG DELIVERY

The application of nanomaterials in drug delivery has revolutionized the pharmaceutical industry by offering more precise, efficient, and targeted methods for delivering therapeutic agents. Nanomaterials can improve the pharmacokinetics, bioavailability, and safety profiles of drugs, allowing for the development of novel therapies, particularly in the fields of oncology, infectious diseases, and chronic conditions.

3.1. Targeted Drug Delivery

Targeted drug delivery is one of the most promising applications of nanomaterials, offering the potential to deliver drugs directly to diseased tissues or cells while minimizing the effects on healthy tissues and reducing side effects. Nanoparticles can be engineered with specific ligands or antibodies that recognize and bind to receptors overexpressed on target cells, such as cancer cells (Yu et al., 2010). Active targeting involves functionalizing nanoparticles with ligands such as antibodies, peptides, or small molecules that bind specifically to receptors on the surface of diseased cells (Salahpour Anarjan, 2019). For example, in cancer therapy, nanoparticles can be modified with folic acid, which targets the folate receptor commonly overexpressed in many types of tumors (Bellotti et al., 2021). This targeted approach allows for the selective accumulation of therapeutic agents at the tumor site, improving drug efficacy while minimizing systemic toxicity (Chehelgerdi et al., 2023). In contrast, passive targeting relies on the Enhanced Permeability and Retention (EPR) effect, which takes advantage of the leaky vasculature and poor lymphatic drainage of tumor tissues (Subhan et al., 2021). Nanoparticles can accumulate preferentially at tumor sites through this effect, increasing the local concentration of chemotherapeutic drugs without the need for specific targeting ligands, making passive targeting especially useful for delivering anticancer treatments (Chehelgerdi et al., 2023).

3.2. Controlled and Sustained Release

Controlled and sustained release of therapeutic agents through nanomaterials offers significant advantages in maintaining consistent drug levels over extended periods, reducing dosing frequency, and improving patient compliance (Adepu & Ramakrishna, 2021; Bai et al., 2022). Polymeric nanoparticles, such as those made from biodegradable materials like PLGA or polycaprolactone, are designed to encapsulate drugs and release them gradually as the polymer degrades within the body (Gagliardi et al., 2021). This mechanism is particularly beneficial for drugs with short half-lives, allowing for prolonged therapeutic effects with fewer doses, which is especially useful for managing chronic diseases like diabetes or cardiovascular conditions (Elmowafy et al., 2023). Controlled-release formulations in these cases help reduce the frequency of administration, improving patient adherence to treatment regimens (Adepu & Ramakrishna, 2021).

Additionally, stimuli-responsive nanoparticles are engineered to release drugs in response to specific physiological conditions or external stimuli such as pH, temperature, or light. These nanoparticles ensure that the drug is released only when it reaches the target site (G. Liu et al., 2020). For instance, pH-responsive nanoparticles can release their drug payload in the acidic environment of a tumor or inflamed tissue, ensuring the drug is delivered precisely where it is needed, minimizing side effects, and enhancing treatment efficacy (Chu et al., 2022).

3.3. Overcoming Biological Barriers

Overcoming Biological Barriers is a critical challenge in drug delivery, as barriers such as the blood-brain barrier (BBB) and gastrointestinal barriers can limit the ability of therapeutic agents to reach certain tissues (Ribovski et al., 2021). Nanomaterials offer innovative solutions to penetrate or bypass these barriers, enabling treatments for conditions that were previously difficult to address (Mohamed et al., 2022). Crossing the BBB is particularly challenging due to its selective nature, which prevents most drugs from entering the brain (D. Wu et al., 2023). Nanoparticles can be engineered to cross the BBB by functionalizing their surfaces with specific ligands that interact with transport mechanisms in brain endothelial cells (Hersh et al., 2022). Lipid-based nanoparticles have shown considerable promise in delivering drugs to treat neurodegenerative diseases such as Alzheimer's and Parkinson's disease, offering a potential breakthrough in treating these conditions (Rahman et al., 2022; Witika et al., 2022).

In addition, nanomaterials enhance oral drug delivery by protecting drugs from degradation in the acidic and enzymatic environment of the gastrointestinal tract, thereby improving bioavailability (Date et al., 2016). Lipid-based nanocarriers, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), encapsulate drugs to protect them from degradation and enhance their absorption through the intestinal mucosa. These carriers are especially useful for improving the bioavailability of poorly water-soluble drugs, ensuring more effective oral therapies (Ghasemiyeh & Mohammadi-Samani, 2018; Mehta et al., 2023).

3.4. Improving Drug Solubility and Bioavailability

Improving drug solubility and bioavailability is a key advantage of nanomaterials in drug delivery, especially for therapeutic compounds with poor solubility, which often limits their clinical efficacy (Y. Liu et al., 2024). Nanomaterials enhance the solubility of hydrophobic drugs, making them more bioavailable and increasing their therapeutic potential (Pinal, 2024). Nanocrystals are one such approach, consisting of pure drug particles reduced to the nanometer scale and stabilized by surfactants (Gigliobianco et al., 2018). By reducing particle size, the surface area is increased, which accelerates the dissolution rate of the drug, thereby improving its solubility and bioavailability (Kumari et al., 2023). Nanocrystal formulations have been used effectively in delivering poorly soluble drugs like paclitaxel, an anticancer agent, and fenofibrate, a lipid-lowering drug, enabling better therapeutic outcomes (Gigliobianco et al., 2018).

Lipid-based nanocarriers such as liposomes, micelles, and solid lipid nanoparticles (SLNs) also play a significant role in improving the solubility of hydrophobic drugs (Mehta et al., 2023). These lipid nanoparticles encapsulate the drug within their lipid bilayer or core, facilitating solubility in biological fluids (Graván et al., 2023). Liposomes, for instance, have been used to encapsulate hydrophobic anticancer drugs like doxorubicin, improving their solubility and making intravenous administration possible (Ibrahim et al., 2022). This encapsulation not only enhances bioavailability but also helps in reducing the systemic toxicity of potent drugs (Mehta et al., 2023).

3.5. Combination Therapy and Multifunctional Nanocarriers

Combination therapy and multifunctional nanocarriers leverage the unique capabilities of nanomaterials to enhance therapeutic effectiveness by delivering multiple agents or combining therapy with diagnostic functions (X. Li et al., 2024). In combination therapy, nanoparticles can carry multiple drugs with complementary or synergistic effects, enabling the simultaneous delivery of agents with different mechanisms of action (Gong et al., 2023; R. X. Zhang et al., 2016). This approach is especially beneficial in cancer therapy, where using a combination of chemotherapeutic drugs can help overcome drug resistance and improve patient outcomes. For example, polymeric nanoparticles can be loaded with both a chemotherapeutic agent and a gene-silencing RNA molecule, delivering a dual attack on cancer cells by simultaneously inhibiting tumor growth and suppressing specific gene expression (Xia et al., 2021).

Theranostics, or multifunctional nanocarriers, take this concept further by incorporating both therapeutic and diagnostic capabilities within a single platform. These nanomaterials can be engineered to deliver drugs while simultaneously providing real-time imaging or diagnostic feedback (Janib et al., 2010). For instance, nanoparticles can be functionalized with both a therapeutic agent and an imaging marker, such as a fluorescent dye or MRI contrast agent, allowing clinicians to track the drug's distribution and assess its effectiveness in real time (Sharma et al., 2024). Gold nanoparticles, which possess both therapeutic and imaging properties, are being explored for photothermal therapy, where they absorb light and generate heat to destroy tumors, and as contrast agents in imaging applications to visualize tumor localization and treatment progress (Vines et al., 2019).

3.6. Personalized Medicine

Personalized medicine is an emerging field in which nanomaterials offer significant potential to tailor treatments based on a patient's unique genetic makeup and disease profile (M. A. Alghamdi et al., 2022). By utilizing nanoparticles customized for specific patients, more precise and effective drug delivery can be achieved. Genomic and proteomic delivery is one area where nanomaterials play a crucial role. Nanoparticles can be used to deliver genetic material, such as DNA or RNA, to specific cells, enabling gene therapy and treatment for genetic disorders (Herranz et al., 2011). A prime example is the use of lipid nanoparticles to deliver mRNA in the COVID-19 vaccines, demonstrating the potential for mRNA-based therapeutics in a wide range of diseases (Swetha et al., 2023). In cancer therapy, nanoparticles are also used to deliver small interfering RNA (siRNA) or microRNA (miRNA) to silence genes that drive tumor growth, offering a powerful tool for precision oncology (Bravo-Vázquez et al., 2023).

Patient-specific targeting further enhances the personalized approach, where nanoparticles are functionalized with targeting ligands that bind to biomarkers unique to an individual patient's disease (Choksi et al., 2022). For instance, in cancer treatment, nanoparticles can be designed to target mutations or receptors that are specific to the patient's tumor. This targeted approach allows for more effective treatment while reducing toxicity and side effects by focusing on diseased cells and sparing healthy tissues, significantly advancing the potential for personalized nanomedicine (Yao et al., 2020).

4. THERAPEUTIC APPLICATIONS of NANOMATERIALS

Nanomaterials are transforming the therapeutic landscape, enabling more targeted, effective, and innovative treatments for various diseases. Their nanoscale size, unique physical and chemical properties, and ability to interact with biological molecules at the cellular and molecular levels allow for enhanced precision in drug delivery, novel therapeutic modalities, and reduced systemic toxicity.

4.1. Cancer Therapy

Nanomaterials have shown immense potential in oncology, improving drug delivery systems, reducing side effects, and introducing novel therapies that increase treatment efficacy.

4.1.1. Targeted Drug Delivery in Cancer

Traditional cancer therapies like chemotherapy often affect both cancerous and healthy cells, leading to severe side effects. Nanomaterials have revolutionized cancer treatment by enabling targeted drug delivery, ensuring that therapeutic agents reach tumor cells while sparing healthy tissues. Nanoparticles such as liposomes, dendrimers, and polymeric nanoparticles can encapsulate chemotherapy drugs, protecting them from degradation in the bloodstream and facilitating controlled release at the tumor site. Drugs like doxorubicin, paclitaxel, and cisplatin are commonly loaded into these nanoparticles. For instance, Doxil (a liposomal formulation of doxorubicin) takes advantage of the Enhanced Permeability and Retention (EPR) effect, where the leaky vasculature of tumors allows nanoparticles to accumulate, increasing drug concentration at the tumor site while reducing cardiotoxicity (Kaminskas et al., 2012). In addition to passive targeting through the EPR effect, active targeting is achieved by functionalizing nanoparticles with ligands such as antibodies, peptides, or small molecules that bind to receptors overexpressed on cancer cells (e.g., folate receptors in ovarian cancer). This active targeting further improves the specificity of drug delivery, enhancing treatment efficacy (Makwana et al., 2021). Monoclonal antibody-functionalized nanoparticles are also being explored to selectively target tumor cells, increasing the precision of cancer therapies.

4.1.2. Photothermal and Photodynamic Therapies (PTT and PDT)

Nanomaterials have introduced innovative cancer treatments like photothermal and photodynamic therapies, providing highly localized treatments with minimal damage to surrounding healthy tissues. Photothermal Therapy (PTT) utilizes gold nanoparticles (AuNPs) due to their strong light absorption properties. When exposed to near-infrared (NIR) light, AuNPs absorb the light and convert it into heat, which selectively destroys cancer cells by raising the local temperature, sparing healthy tissues. This technique is particularly effective for treating superficial tumors, such as skin cancers, and can also be applied to deeper tumors using advanced laser systems. PTT can be combined with traditional chemotherapy to enhance treatment outcomes, providing a dual approach to cancer therapy (Dastgheib et al., 2024; Hlapisi et al., 2024).

On the other hand, Photodynamic Therapy (PDT) uses nanoparticles to deliver photosensitizing agents to tumors, which generate reactive oxygen species (ROS) when exposed to light, causing cancer cell death. Nanoparticles like silica-based carriers and quantum dots improve the targeting of photosensitizers, increasing their concentration in cancer cells while reducing damage to healthy tissues. PDT is being investigated for treating various cancers, including bladder, head and neck, and esophageal cancers, offering a more focused and less invasive alternative to conventional therapies (Singh et al., 2024).

4.1.3. Gene Therapy and RNA Interference (RNAi)

Nanomaterials play a pivotal role in delivering genetic therapies, such as siRNA (small interfering RNA) or mRNA, which can modulate gene expression in cancer cells. RNA interference

(RNAi) for gene silencing leverages nanoparticles, often composed of lipids or polymers, to encapsulate siRNA molecules. These siRNA molecules are designed to silence specific oncogenes responsible for driving cancer growth. By delivering siRNA directly to cancer cells, nanoparticles enable the downregulation of harmful genes, offering a promising new approach for precision medicine (Gomes-da-Silva et al., 2012). Lipid-based nanoparticles, in particular, have shown success in clinical trials, targeting diseases such as liver cancer and metastatic tumors, highlighting their potential in treating various cancers (Mainini & Eccles, 2020).

mRNA-based therapies also utilize lipid nanoparticles (LNPs) to deliver mRNA therapeutics that instruct cells to produce therapeutic proteins or antigens. This method is being actively explored in cancer vaccines, where the mRNA encodes tumor-associated antigens, prompting an immune response that specifically targets cancer cells (T. Huang et al., 2022). Advances in this field have demonstrated the ability of LNPs to enhance the stability and delivery efficiency of mRNA, thus expanding the scope of gene therapy applications in oncology (Guevara et al., 2020). These advances in gene therapy and RNAi are pushing the boundaries of cancer treatment, providing highly targeted and personalized approaches to combat the disease.

4.2. Regenerative Medicine

Nanomaterials are making significant strides in regenerative medicine by aiding tissue repair and organ regeneration. Their ability to mimic biological structures and promote cell growth makes them ideal for tissue engineering and wound healing.

4.2.1. Nanofibers and Scaffolds for Tissue Engineering

Electrospun nanofibers provide scaffolds that closely mimic the extracellular matrix (ECM), offering structural support essential for cell adhesion, proliferation, and differentiation (Abdou et al., 2024). These scaffolds are typically made from biodegradable polymers such as polylactic acid (PLA), polycaprolactone (PCL), and collagen, which gradually degrade as new tissue forms (Shanmugam, 2024). Tissue-specific scaffolds are used to engineer various types of tissues, including skin, bone, cartilage, and nerves. For instance, in skin tissue engineering, nanofibers create an ideal environment for keratinocytes and fibroblasts to regenerate damaged skin. In bone regeneration, nanofibers made from materials like calcium phosphate or bioactive glass promote osteoblast adhesion, encouraging new bone formation (Dilmani et al., 2024).

Additionally, nanomaterials enhance growth factor and stem cell delivery to damaged tissues. Nanofiber scaffolds can be loaded with growth factors such as vascular endothelial growth factor (VEGF) or basic fibroblast growth factor (bFGF), which stimulate blood vessel formation (angiogenesis) and support tissue repair (Subbiah & Guldborg, 2019). Moreover, nanoparticles can deliver mesenchymal stem cells (MSCs) to injured tissues, enhancing their regenerative potential by facilitating tissue healing and promoting the regeneration of specific cell types (Raghav et al., 2022). These advances in nanofibers and scaffolds are transforming tissue engineering and regenerative medicine.

4.2.2. Hydrogels with Nanoparticles for Controlled Release

Nanoparticle-embedded hydrogels are widely utilized for controlled drug delivery and tissue repair, providing a moist, protective environment conducive to wound healing while enabling the gradual release of therapeutic agents. Wound healing applications often incorporate silver nanoparticles (AgNPs) into hydrogels for their antimicrobial properties, making these hydrogels particularly effective for preventing infections and promoting faster wound closure (Kalantari et al., 2020). Such nanoparticle-based hydrogels are being developed for difficult-to-heal wounds, such as diabetic foot ulcers and chronic wounds, offering both protection and accelerated healing (Dam et al., 2023).

In bone and cartilage regeneration, nanocomposite hydrogels that include nanoparticles like hydroxyapatite or bioactive glass offer additional mechanical strength while also releasing

bioactive molecules that stimulate tissue growth. These hydrogels serve as scaffolds for regenerating bone and cartilage, providing structural support and aiding the natural repair processes of the body (Kumar & Han, 2021). Through the combination of nanoparticles and hydrogels, these materials represent a significant advance in regenerative medicine and controlled drug delivery systems (Abd El-Aziz et al., 2021).

4.3. Antimicrobial and Antiviral Therapy

The rise of antimicrobial resistance has spurred significant interest in nanomaterials for infection treatment, especially for infections resistant to traditional antibiotics. Nanoparticles serve both as antimicrobial agents and as carriers for existing drugs, enhancing their efficacy. Among these, silver nanoparticles (AgNPs) are widely studied for antimicrobial applications due to their broad-spectrum activity against bacteria, viruses, and fungi. AgNPs exert their antimicrobial effects by disrupting bacterial cell membranes, generating reactive oxygen species (ROS), and binding to bacterial DNA to inhibit replication (Joshi et al., 2020). These nanoparticles have been incorporated into wound dressings, medical device coatings, and disinfectant sprays, all of which help reduce infection risks in healthcare settings. Additionally, nanoparticles can enhance the effectiveness of traditional antibiotics. For instance, gold or silver nanoparticles conjugated with antibiotics can improve drug delivery to bacterial cells, overcoming antibiotic resistance mechanisms like biofilm formation (Ahsan et al., 2024).

Nanoparticles are also being explored for their antiviral potential, targeting viruses such as HIV, influenza, and hepatitis. Functionalized gold nanoparticles (AuNPs) have shown promise in antiviral therapy by binding to viral proteins or host cell receptors, thereby preventing the virus from entering cells (Gkartziou et al., 2021). Furthermore, lipid nanoparticles (LNPs) have been instrumental in vaccine development, especially in mRNA vaccines like the COVID-19 vaccines from Pfizer-BioNTech and Moderna. These LNPs protect mRNA from degradation, facilitate its cellular delivery, and enhance immune responses by presenting antigens that elicit protective immunity (Jiang et al., 2020). The use of nanotechnology in combating antimicrobial resistance and supporting vaccine development represents a transformative advancement in addressing infectious diseases.

4.4. Neurological Disorders

Treating neurological diseases is challenging due to the blood-brain barrier (BBB), which prevents many drugs from reaching the brain. Nanomaterials are being developed to cross the BBB, providing a way to deliver therapeutic agents directly to the central nervous system (CNS) (Chauhan et al., 2024). Lipid-based and polymeric nanoparticles can cross the BBB by engaging specific transport mechanisms, such as receptor-mediated endocytosis, allowing for effective drug delivery in neurodegenerative diseases like Alzheimer's and Parkinson's (Vahab et al., 2024). Nanoparticles can also be functionalized with ligands that bind to receptors on the surface of brain endothelial cells, which facilitates their transport across the BBB. For example, transferrin-functionalized nanoparticles have been designed to deliver neuroprotective drugs directly to the brain to combat neurodegenerative diseases (Mahanta et al., 2024).

Furthermore, nanoparticles enable the targeted delivery of neuroprotective agents, antioxidants, and anti-inflammatory drugs to the brain. This targeted approach can mitigate neuroinflammation and oxidative stress, both of which are critical factors in the progression of neurodegenerative diseases (Genchi et al., 2024). These advancements in nanotechnology open new possibilities for treating complex CNS conditions, offering hope for more effective interventions.

4.5. Cardiovascular Diseases

Nanomaterials are being explored for treating cardiovascular conditions such as atherosclerosis, myocardial infarction (heart attacks), and restenosis (re-narrowing of arteries after surgery). Nanoparticles can deliver drugs that target atherosclerotic plaques, preventing their progression or promoting their

regression (Y. Wu et al., 2021). These nanoparticles, such as liposomes or polymeric nanoparticles, can be loaded with anti-inflammatory drugs, cholesterol-lowering agents, or antioxidants and directed to inflamed atherosclerotic plaques, which helps reduce plaque size and prevent further buildup, ultimately lowering the risk of heart attacks and strokes (Haba et al., 2021). Additionally, theranostic nanoparticles, which combine diagnostic and therapeutic functions, are being developed to image atherosclerotic plaques while simultaneously delivering drugs to prevent plaque rupture. This theranostic approach allows for real-time monitoring of treatment efficacy, making it a valuable tool in cardiovascular disease management (Bejarano et al., 2018).

Nanomaterials are also being investigated for their potential to regenerate damaged heart tissue following a heart attack. Gold nanoparticles and carbon nanotubes are being incorporated into scaffolds that promote the growth of cardiomyocytes (heart cells) and improve cardiac function post-myocardial infarction. These scaffolds provide essential structural support for regenerating heart tissue and enhance the electrical conductivity needed for synchronized heart contractions (Setia et al., 2023). Through the combination of nanoparticles and scaffolds, these materials represent significant advancements in regenerative medicine, specifically for cardiovascular applications.

4.6. Nanoparticle-Based Drugs and Drug Delivery Systems Incorporating Nanoparticles

The ability of nanoparticles to encapsulate and transport drugs directly to disease sites has led to the development of several successful nanoparticle-based drugs, especially in cancer therapy, and chronic conditions. These innovative formulations ensure that the drugs are released precisely where needed, often improving patient outcomes and reducing systemic toxicity. A list of some prominent nanoparticle-delivered drugs that have made a significant impact in clinical medicine are presented in Table 1.

4.6.1. Doxil

Doxil (Liposomal Doxorubicin) is one of the most well-known nanoparticle-based drugs, used to treat various cancers, including ovarian cancer, multiple myeloma, and AIDS-related Kaposi's sarcoma (Duggan & Keating, 2011). It is a liposomal formulation of the chemotherapeutic agent doxorubicin (Soundararajan et al., 2009). Doxil takes advantage of the Enhanced Permeability and Retention (EPR) effect, which allows liposomes to accumulate preferentially in tumor tissues due to their leaky vasculature (Parveen et al., 2012). This targeted delivery system significantly reduces the cardiotoxicity typically associated with doxorubicin, making it safer for long-term cancer treatment (Aldughaim et al., 2020).

4.6.2. Abraxane

Abraxane (Nanoparticle Albumin-Bound Paclitaxel) is used primarily to treat breast cancer, non-small cell lung cancer (NSCLC), and pancreatic cancer (Ma & Mumper, 2013). Abraxane is a nanoparticle formulation in which the chemotherapy drug paclitaxel, which is hydrophobic and poorly soluble, is bound to albumin nanoparticles (Zhao et al., 2015). These nanoparticles improve the solubility of paclitaxel and enhance its delivery to tumors via natural albumin transport mechanisms (S. Lu et al., 2025). This formulation eliminates the need for toxic solvents, reduces hypersensitivity reactions, and allows for higher dosing of paclitaxel, which leads to improved therapeutic outcomes (Roy et al., 2009).

4.6.3. Onivyde

Onivyde (Liposomal Irinotecan) is used to treat metastatic pancreatic cancer, often in combination with other agents (Cui et al., 2024; Lamb & Scott, 2017). It is a liposomal formulation of irinotecan, a chemotherapy drug that inhibits topoisomerase (Milano et al., 2022). Encapsulation within liposomes enhances the stability of irinotecan in the bloodstream and facilitates its accumulation at the tumor site (Tran et al., 2017). This approach ensures sustained drug release at the tumor, improving

bioavailability and reducing systemic side effects, providing a more effective treatment option for difficult-to-treat cancers such as metastatic pancreatic cancer (Kciuk et al., 2020).

4.6.4. Vyxeos

Vyxeos (CPX-351) is an innovative drug approved for the treatment of acute myeloid leukemia (AML) (Alfayez et al., 2020). It is a liposomal formulation that co-encapsulates two chemotherapy drugs, daunorubicin and cytarabine, in a fixed 5:1 molar ratio (Dicko et al., 2010). This co-delivery system allows for simultaneous delivery of both drugs directly to the tumor, leveraging the EPR effect for targeted delivery (Lancet et al., 2014). Vyxeos® improves overall survival rates in AML patients by enhancing the synergy between these two drugs while reducing systemic toxicity (Alfayez et al., 2020).

4.6.5. Rapamune

Rapamune (Sirolimus) is used to prevent organ rejection in kidney transplant patients (Augustine et al., 2007). It is a nanoparticle-based formulation of sirolimus, an immunosuppressive drug with poor water solubility. Nanoparticle technology improves the solubility and bioavailability of sirolimus, allowing for more consistent and controlled drug levels in the bloodstream (Haeri et al., 2018). This formulation leads to more effective immunosuppression, providing better transplant outcomes with fewer side effects (Asleh et al., 2022).

4.6.6. Aurimmune

Aurimmune (Cyt-6091), currently in clinical trials, is a promising gold nanoparticle system that delivers the cytokine tumor necrosis factor-alpha (TNF- α) directly to tumors for cancer treatment (Kotcherlakota et al., 2019; Shao et al., 2013). The gold nanoparticles act as carriers for TNF- α , targeting tumors and inducing immune responses to kill cancer cells (Kotcherlakota et al., 2019). This targeted delivery system reduces the systemic toxicity typically associated with TNF- α while enhancing its therapeutic efficacy (Dimitriou et al., 2017).

4.6.7. Marqibo

Marqibo (Vincristine Sulfate Liposome Injection) is used in the treatment of acute lymphoblastic leukemia (ALL) (Raj et al., 2013). It is a liposomal formulation of vincristine, a chemotherapy drug. By encapsulating vincristine in liposomes, Marqibo allows for sustained release of the drug at the tumor site, reducing the systemic side effects and neurotoxicity commonly associated with vincristine (Harrison & Lyseng-Williamson, 2013; Silverman & Deitcher, 2013). This targeted delivery improves the drug's efficacy in treating leukemia (N. N. Shah et al., 2016).

4.6.8. DepoCyt

DepoCyt (Liposomal Cytarabine) is used for the treatment of lymphomatous meningitis (Benesch & Urban, 2008). It is a sustained-release liposomal formulation of cytarabine designed for intrathecal (spinal) administration (Domínguez et al., 2005). The liposomal encapsulation ensures prolonged exposure of cytarabine to the meninges, improving its efficacy in the treatment of central nervous system lymphomas (Kripp & Hofheinz, 2008). DepoCyt® also reduces the frequency of dosing, making it more convenient for patients (Jaeckle et al., 2002).

4.6.9. Feraheme

Feraheme (Ferumoxytol) is used to treat iron deficiency anemia, particularly in patients with chronic kidney disease (CKD) (Kowalczyk et al., 2011). It is an iron oxide nanoparticle formulation that not only serves as an iron replacement therapy but also has potential use as an MRI contrast agent due to its magnetic properties (Hood et al., 2019; Mukundan et al., 2016). Feraheme provides faster and more efficient iron replenishment compared to oral supplements, with fewer gastrointestinal side effects. Additionally, its potential for use as an MRI contrast agent adds versatility to its clinical application (Stoumpos et al., 2019).

5. APPLICATIONS of NANOMATERIALS in DIAGNOSTICS

Nanomaterials have shown remarkable potential in improving the precision, sensitivity, and speed of diagnostics. Their unique properties, such as high surface area, tunable optical and magnetic behaviors, and ability to interact with biomolecules at the nanoscale, make them ideal candidates for early disease detection, biomarker identification, and medical imaging.

5.1. Imaging Technologies

Nanomaterials have significantly advanced medical imaging by enhancing resolution, contrast, and specificity, which has improved early detection and disease monitoring, particularly in oncology and neurology (Dulińska-Litewka et al., 2019). Quantum dots (QDs), semiconductor nanocrystals, emit fluorescence when exposed to light and offer advantages such as higher brightness, resistance to photobleaching, and adjustable emission wavelengths by changing their size. QDs are extensively used in molecular imaging, where they enable real-time tracking of cellular processes (D. Chen et al., 2017). For example, by attaching targeting ligands to QDs that bind to cancer-specific markers, highly sensitive cancer detection is possible. Superparamagnetic iron oxide nanoparticles (SPIONs) serve as contrast agents in magnetic resonance imaging (MRI), where their superparamagnetic properties enhance image contrast and improve the detection of tumors, inflammation, and vascular disorders (Nguyen et al., 2018). Functionalizing SPIONs with targeting ligands allows them to accumulate in specific tissues or tumor sites, enhancing diagnostic accuracy, particularly in cancer and neurological conditions. Gold nanoparticles play a vital role in photoacoustic imaging, a hybrid technique combining light and ultrasound to produce high-resolution images (Javed et al., 2019). These nanoparticles absorb light and convert it to heat, creating acoustic signals detectable by ultrasound, making them particularly useful for imaging tumors or identifying vascular abnormalities. Additionally, gold nanoparticles are employed in Surface-Enhanced Raman Scattering (SERS), a technique that amplifies the Raman signals of biomolecules, enabling highly sensitive biomolecular detection when they are in close proximity to the nanoparticles (Kim & Jeong, 2017).

5.2. Biosensors and Diagnostic Assays

Nanomaterials have significantly improved the performance of biosensors, which are devices designed to detect specific biological molecules, such as proteins, DNA, or glucose, and convert their presence into measurable signals. The high surface area of nanomaterials enhances the sensitivity and response times of these sensors, allowing them to detect minute quantities of biomarkers, leading to earlier and more accurate diagnoses

(Pasinszki et al., 2017). Gold nanoparticles are commonly used in lateral flow assays (LFAs), such as the widely known home pregnancy test. In these assays, gold nanoparticles are conjugated to antibodies or other recognition molecules. When a specific biomarker is present in a sample, such as urine or blood, the nanoparticles bind to it and produce a visible color change on the test strip, making them adaptable for rapid tests for infectious diseases, including COVID-19 (Rivas et al., 2017). Carbon nanotube-based biosensors are another example, where the unique electrical properties of carbon nanotubes (CNTs) enable the detection of biomolecules like glucose, cholesterol, and DNA with high sensitivity. These sensors are being developed for applications such as continuous glucose monitoring in diabetic patients and the detection of genetic mutations associated with cancer (B. Wang et al., 2017). Additionally, nanowires, typically made from silicon or other semiconductors, are employed in highly sensitive biosensors that detect biomolecules at very low concentrations. Nanowire-based field-effect transistors (FETs) can detect the binding of biomolecules to the nanowire surface, altering the electrical properties of the device, useful in the detection of disease biomarkers, environmental monitoring, and food safety testing (Rusling et al., 2009).

5.3. Biomarker Detection and Disease Diagnosis

Nanomaterials are driving significant advancements in the detection of biomarkers—molecules that signal the presence or progression of a disease. Early and accurate biomarker detection is crucial for diagnosing diseases at their earliest stages, often before symptoms appear. Nanoparticle-based ELISA (Enzyme-Linked Immunosorbent Assay) is one such advancement. Traditional ELISA is widely used to detect specific proteins or antibodies in a sample, but by incorporating nanoparticles, such as gold nanoparticles or quantum dots, the sensitivity of ELISA is significantly enhanced (Huda et al., 2021). These nanoparticle-enhanced ELISAs amplify detection signals, enabling the identification of lower concentrations of biomarkers, which makes it an effective tool for early diagnosis of diseases like cancer, HIV, and autoimmune disorders (M. F. Alghamdi & Redwan, 2021). Another critical application is in exosome detection. Exosomes are tiny vesicles released by cells that carry proteins, lipids, and genetic material, making them important biomarkers for diseases like cancer and neurodegenerative conditions. Nanomaterials such as magnetic nanoparticles or gold nanoparticles are used to isolate and analyze exosomes from blood or urine samples, improving the speed and sensitivity of detection (Boriachek et al., 2018). Nanoparticle-based techniques allow for the identification of disease-specific exosome markers, facilitating early diagnosis and disease monitoring.

Table 1: Drug delivery systems incorporating nanoparticles, their indications, technologies, and advantages

Drug Name	Indication	Technology	Advantages	References
Doxil	Ovarian cancer, multiple myeloma, AIDS-related Kaposi's sarcoma	Liposomal formulation of doxorubicin	Reduced cardiotoxicity, targeted delivery via EPR effect	(Aldughaim et al., 2020; Duggan & Keating, 2011; Parveen et al., 2012; Soundararajan et al., 2009)
Abraxane	Breast cancer, non-small cell lung cancer, pancreatic cancer	Nanoparticle albumin-bound paclitaxel	No toxic solvents, improved solubility, enhanced tumor delivery	(S. Lu et al., 2025; Ma & Mumper, 2013; Roy et al., 2009; Zhao et al., 2015)
Onivyde	Metastatic pancreatic cancer	Liposomal irinotecan	Improved stability and bioavailability, reduced side effects	(Cui et al., 2024; Kciuk et al., 2020; Lamb & Scott, 2017; Tran et al., 2017).
Vyxeos	Acute myeloid leukemia (AML)	Liposomal co-encapsulation of daunorubicin and cytarabine	Improved survival rates in AML, reduced systemic toxicity	(Alfayez et al., 2020; Dicko et al., 2010; Lancet et al., 2014).
Rapamune	Preventing organ rejection in kidney transplant patients	Nanoparticle-based formulation of sirolimus	Improved bioavailability and consistent drug levels	(Asleh et al., 2022; Augustine et al., 2007; Haeri et al., 2018)
Aurimmune	Cancer treatment (clinical trials)	Gold nanoparticle delivering TNF- α	Targeted delivery, reduced systemic toxicity	(Dimitriou et al., 2017; Kotcherlakota et al., 2019).
Marqibo	Acute lymphoblastic leukemia (ALL)	Liposomal vincristine sulfate	Sustained release, reduced neurotoxicity	(Harrison & Lyseng-Williamson, 2013; Raj et al., 2013; N. N. Shah et al., 2016; Silverman & Deitcher, 2013)
DepoCyt	Lymphomatous meningitis	Liposomal cytarabine	Prolonged drug exposure, reduced dosing frequency	(Benesch & Urban, 2008; Domínguez et al., 2005; Jaecckle et al., 2002; Kripp & Hofheinz, 2008)
Feraheme	Iron deficiency anemia (CKD patients)	Iron oxide nanoparticle	Faster iron replenishment, fewer gastrointestinal side effects	(Hood et al., 2019; Kowalczyk et al., 2011; Mukundan et al., 2016; Stoumpos et al., 2019).

5.4. Point-of-Care Diagnostics

Nanomaterials are facilitating the development of portable, rapid, and easy-to-use diagnostic devices for point-of-care (POC) applications, which are particularly valuable in resource-limited settings or for managing infectious diseases. These technologies allow for timely diagnosis, enabling quick treatment and containment of outbreaks (Alam et al., 2023). Nanoparticle-based rapid tests are a prime example, where gold nanoparticles are commonly used in lateral flow assays to provide diagnostic results within minutes, without the need for specialized laboratory equipment. For instance, during the COVID-19 pandemic, gold nanoparticle-based rapid antigen tests were widely deployed to detect SARS-CoV-2, offering accessible and quick testing that played a crucial role in controlling the virus's spread (Dorta-Gorrín et al., 2023). Additionally, paper-based microfluidic devices are being enhanced with nanomaterials, offering an inexpensive and portable diagnostic solution. These devices rely on capillary action to move liquid samples, such as blood or saliva, through embedded nanoparticles or biosensors on the paper, enabling complex diagnostics. This technology is being developed for use in regions with limited healthcare infrastructure, providing rapid testing for infectious diseases like malaria, tuberculosis, and HIV, and expanding access to critical healthcare diagnostics (Nishat et al., 2021).

5.5. Diagnostics systems incorporating nanoparticles

Nanomaterials have led to the development of highly effective diagnostic platforms, offering superior sensitivity, specificity, and rapid detection. These systems incorporate various types of nanomaterials, such as gold nanoparticles, quantum dots, and superparamagnetic nanoparticles, to detect diseases early and accurately (Table 2).

5.5.1. Verigene System

The Verigene System uses gold nanoparticle-based technology to detect pathogens, including bacteria and viruses, directly from blood samples. It utilizes DNA or RNA probes functionalized with gold nanoparticles that bind to target sequences, allowing for the rapid identification of infectious agents (Cellini et al., 2015). This system is especially valuable in diagnosing sepsis, where quick detection of pathogens can lead to timely and appropriate treatment, significantly improving patient outcomes (Berkold et al., 2017). The Verigene System's ability to rapidly identify pathogens, combined with its accuracy, has shown significant impact in clinical settings, particularly in critical conditions like sepsis (Peri et al., 2021).

5.5.2. T2 Biosystems

T2 Biosystems employs superparamagnetic nanoparticles for the rapid detection of sepsis-causing pathogens directly from whole blood. Using magnetic resonance (T2MR) technology, these nanoparticles bind to microbial DNA, and the binding event alters the magnetic resonance signal, allowing for quick pathogen identification without the need for traditional blood

cultures (Neely et al., 2013). This system is crucial for diagnosing life-threatening infections like sepsis within hours instead of days, facilitating faster and more effective treatment (De Angelis et al., 2018). This approach, using T2MR technology, has demonstrated substantial accuracy and impact on clinical outcomes by reducing the diagnostic time and enabling timely intervention (Paggi et al., 2021).

5.5.3. i-STAT System

The i-STAT System by Abbott is a handheld blood analyzer that incorporates nanoparticles to perform a variety of diagnostic tests, such as blood gases, electrolytes, and cardiac biomarkers. This point-of-care diagnostic tool is used in emergency departments and critical care units to rapidly assess patients and make real-time clinical decisions. The nanoparticle-enhanced technology improves the sensitivity and accuracy of these assays, helping clinicians respond quickly to critical situations (Buño et al., 2008).

5.5.4. Surface-Enhanced Raman Scattering (SERS) Biosensors

Surface-Enhanced Raman Scattering (SERS) Biosensors use gold or silver nanoparticles to amplify the Raman signals emitted by biomolecules near the nanoparticles' surface. SERS offers exceptional sensitivity, allowing for the detection of disease biomarkers at ultra-low concentrations. This technology is useful for early diagnosis of conditions like cancer and infectious diseases, where detecting trace amounts of disease-related molecules is crucial for timely intervention (Proniewicz, 2024).

5.5.5. ExoDx Prostate (IntelliScore) Test

For non-invasive cancer screening, the ExoDx Prostate (IntelliScore) Test uses nanoparticle-based detection to analyze exosomes, which are vesicles secreted by cells containing proteins and RNA that serve as biomarkers for prostate cancer. This urine test identifies specific RNA biomarkers found in exosomes, providing a risk score for high-grade prostate cancer. The ExoDx test is an important tool for reducing unnecessary biopsies and guiding treatment decisions, improving patient care in prostate cancer management (Saliccia et al., 2023; Wei et al., 2023).

5.5.6. Nucleic Acid Lateral Flow Immunoassay (NALFIA)

The Nucleic Acid Lateral Flow Immunoassay (NALFIA) utilizes gold nanoparticles to detect amplified nucleic acid sequences in a point-of-care setting. This system is widely used to rapidly detect various pathogens, including malaria, tuberculosis, and COVID-19. The amplified nucleic acid binds to the gold nanoparticle probes, providing a visual signal that confirms the presence of the pathogen. NALFIA systems are particularly valuable in resource-limited settings where fast, reliable diagnostic results are crucial (Andryukov, 2020; Rubio-Monterde et al., 2023).

Table 2: Diagnostics systems incorporating nanoparticles, the technologies, applications, and advantages of each system.

Diagnostic System	Technology	Application	Advantages	references
Verigene System	Gold nanoparticle-based DNA/RNA probes	Rapid detection of bacterial and viral pathogens in blood	Faster pathogen detection, improved treatment outcomes in sepsis	(Berkold et al., 2017; Cellini et al., 2015; Peri et al., 2021).
T2 Biosystems	Superparamagnetic nanoparticles for pathogen detection	Rapid sepsis pathogen detection without blood cultures	Rapid identification of pathogens, reducing sepsis diagnosis time	(De Angelis et al., 2018; Neely et al., 2013; Paggi et al., 2021).
i-STAT System	Nanoparticles in handheld blood analyzers	Point-of-care diagnostics for blood gases, electrolytes, and cardiac biomarkers	Real-time diagnostics at the patient's bedside, faster clinical decisions	(Buño et al., 2008)
SERS Biosensors	Gold or silver nanoparticles for Raman signal amplification	Ultra-sensitive detection of biomarkers for diseases like cancer	Highly sensitive biomarker detection at very low concentrations	(Proniewicz, 2024)
ExoDx Prostate (IntelliScore) Test	Nanoparticle-based detection of exosome biomarkers	Non-invasive urine test for detecting prostate cancer risk	Non-invasive, reduces need for unnecessary prostate biopsies	(Saliccia et al., 2023; Wei et al., 2023)
Nucleic Acid Lateral Flow Immunoassay (NALFIA)	Gold nanoparticle probes for amplified nucleic acid detection	Rapid detection of pathogens in resource-limited settings for diseases like malaria and COVID-19	Rapid, specific results ideal for point-of-care in low-resource areas	(Andryukov, 2020; Rubio-Monterde et al., 2023)

6. NANOMATERIALS in VACCINE DEVELOPMENT

Nanomaterials have revolutionized vaccine development, offering new ways to enhance the efficacy, stability, and delivery of vaccines. Their ability to mimic natural pathogens, improve antigen delivery, and stimulate strong immune responses has made nanotechnology a key player in next-generation vaccines, including mRNA vaccines and viral vector vaccines.

6.1. Lipid Nanoparticles (LNPs)

Lipid nanoparticles (LNPs) have become central to modern vaccine development, particularly in nucleic acid-based vaccines like mRNA vaccines. Their ability to safely and effectively deliver fragile genetic material has been critical in the success of recent vaccines. For example, LNPs played a pivotal role in the development of mRNA vaccines for COVID-19, such as the Pfizer-BioNTech and Moderna vaccines. These vaccines rely on LNPs to encapsulate and protect the mRNA, preventing degradation and ensuring that the genetic material reaches target cells (Noor, 2021; Polykretis, 2022).

The mechanism by which LNPs function as delivery vehicles is related to their structural similarity to cell membranes. Once in the body, LNPs fuse with cell membranes, releasing the mRNA into the cytoplasm. Here, the cell's machinery translates the mRNA into viral proteins, which the immune system recognizes as foreign, triggering an immune response that includes the generation of antibodies and T cell activation (C. Li et al., 2022). LNPs offer several advantages in vaccine formulation. By stabilizing fragile mRNA, they enhance cellular uptake and amplify immune responses. Unlike traditional vaccines, which often require adjuvants to boost immunity, LNPs inherently support immune activation by directly delivering mRNA into cells. In the case of COVID-19, LNPs facilitated rapid vaccine development, supporting scalable production and efficient distribution (Verbeke et al., 2022).

6.2. Polymer-Based Nanoparticles

Polymeric nanoparticles play a significant role in delivering vaccine antigens or genetic material, offering controlled release and enhancing immune responses. These nanoparticles, often made from poly-lactic-co-glycolic acid (PLGA), can encapsulate antigens and release them slowly over time, generating a sustained immune response (Kunkel & McHugh, 2024). This controlled release is crucial for vaccines targeting diseases where repeated dosing poses a challenge. Moreover, polymeric nanoparticles protect antigens from degradation, ensuring they reach their target intact (Wibowo et al., 2021).

In addition to delivering antigens, polymeric nanoparticles can act as adjuvants, which enhance the body's immune response to an antigen. By combining the antigen and adjuvant within a single nanoparticle, a stronger and longer-lasting immune response is achieved (Allahyari & Mohit, 2016). This dual function enhances the efficacy of the immune response and provides a robust defense against pathogens.

Applications of polymeric nanoparticles are being extensively studied for vaccines against infectious diseases such as HIV, influenza, and tuberculosis. Their versatility, controlled release capabilities, and ability to deliver both proteins and genetic material make them a highly adaptable platform for various vaccine formulations (Jha & Pathak, 2022; Zare et al., 2021).

6.4. Gold Nanoparticles

Gold nanoparticles (AuNPs) are under investigation for their potential to enhance vaccine efficacy by serving as carriers for antigens or adjuvants. AuNPs can be functionalized with antigens, allowing them to deliver these directly to immune cells. Due to their high surface area and customizable surface properties, AuNPs are capable of carrying multiple antigens or adjuvants, making them suitable for multivalent vaccines targeting different strains of a pathogen or multiple pathogens at once (Dykman, 2020). Additionally, gold nanoparticles themselves can act as adjuvants, enhancing immune response. When combined with specific antigens, AuNPs improve the activation of antigen-presenting cells, such as dendritic cells,

leading to stronger and more targeted immune responses (Mateu Ferrando et al., 2020).

Applications of AuNPs are being explored for vaccines against diseases such as malaria, HIV, and influenza. Their ability to enhance immune responses, combined with their biocompatibility, makes them promising candidates for future vaccine development (Carabineiro, 2017; Vieira et al., 2024).

6.5. Nanomaterial-Based Adjuvants

In vaccine development, nanomaterials serve as potent adjuvants that enhance immune responses by activating various immune system components. Aluminum-based nanoparticles (alum) have been used as adjuvants for decades; recent advancements in nanotechnology are enhancing their capacity to stimulate immune responses, particularly in improving antigen uptake and activation of immune cells (M. Li et al., 2022). Silica nanoparticles are also effective as adjuvants, as they enhance antigen uptake by dendritic cells, thereby promoting a stronger immune response (Sun & Xia, 2016). Another promising adjuvant is carbon nanotubes (CNTs), which facilitate the uptake of antigens by immune cells, thus improving T-cell activation and the overall immune response (Ahmed et al., 2024).

Nanomaterial-based adjuvants offer the advantage of enhancing both innate and adaptive immune responses. These adjuvants increase vaccine efficacy by enabling lower antigen doses while still achieving a strong immune response, which is especially beneficial during pandemics when rapid vaccine production is required (Zhu et al., 2014).

6.6. Nanoparticles in DNA Vaccines

Nanoparticles are being used to enhance DNA vaccine platforms, which involve delivering plasmid DNA encoding a viral or bacterial antigen into host cells. These nanoparticles protect the DNA from degradation and enhance cellular uptake, allowing for effective delivery. Once inside the cell, the plasmid DNA is transcribed and translated to produce the antigen, which is then presented to the immune system, triggering a strong immune response (Lee et al., 2018; Pattnaik et al., 2023).

DNA vaccines are under development for several infectious diseases, including the Zika virus, dengue, and various cancers. The use of nanoparticles improves the delivery efficiency of DNA vaccines, helping make these vaccines more feasible for clinical applications. For instance, DNA vaccines combined with nanoparticles show enhanced efficacy in animal models for these diseases, offering promise for broader applications (Hraber et al., 2018; Taslem Mourosi et al., 2022).

6.7. Vaccines incorporates nanoparticles

Vaccines, such as Novavax COVID-19 Vaccine (NVX-CoV2373), NanoFlu (Influenza Vaccine), SpFN (Spike Ferritin Nanoparticle COVID-19 Vaccine), and RTS,S/AS01 (Mosquirix - Malaria Vaccine), showcase the versatility and potential of nanoparticles in addressing various infectious diseases (Table 3).

6.7.1. Novavax COVID-19 Vaccine (NVX-CoV2373)

The Novavax COVID-19 Vaccine (NVX-CoV2373) is a recombinant protein-based nanoparticle vaccine designed to protect against SARS-CoV-2, the virus causing COVID-19. Unlike mRNA vaccines, NVX-CoV2373 uses a stabilized spike protein generated through recombinant nanoparticle technology. This protein is assembled into nanoparticles, enhancing immune system recognition. The vaccine includes a saponin-based Matrix-M adjuvant, which further boosts immune responses by promoting antigen presentation (Organization, n.d.). In clinical trials, NVX-CoV2373 demonstrated a strong efficacy profile, with an estimated 89.7% efficacy against the original SARS-CoV-2 strain and variants (Malabadi et al., 2021). The Matrix-M adjuvant plays a critical role in enhancing immunity by stimulating both humoral and cell-mediated responses, making it particularly effective against symptomatic COVID-19 (Yadav et al., 2023). Given its stability profile, NVX-CoV2373 can be stored at standard refrigeration temperatures, easing distribution and logistics compared to mRNA vaccines, which require ultra-cold storage. This makes NVX-CoV2373 a viable option for

broader distribution, especially in regions with limited cold-chain infrastructure (Lundstrom, 2023).

6.7.2. NanoFlu (Influenza Vaccine)

The NanoFlu (Influenza Vaccine) is a recombinant nanoparticle-based influenza vaccine developed by Novavax, designed to enhance immune responses to seasonal influenza. NanoFlu incorporates recombinant hemagglutinin (HA) proteins from the influenza virus, assembled into nanoparticle structures to increase immunogenicity and stability. The vaccine also uses Novavax's proprietary Matrix-M™ adjuvant, which is derived from saponins and enhances the immune response by promoting antigen presentation to immune cells (Sia et al., 2021).

One of the key advantages of NanoFlu is its stability and robust immune response against various influenza strains, addressing limitations seen in traditional egg-based influenza vaccines. In clinical trials, NanoFlu demonstrated increased immunogenicity compared to traditional influenza vaccines, with significant efficacy in generating antibody responses against both homologous and heterologous strains (Khalaj-Hedayati et al., 2020). Moreover, the nanoparticle structure of NanoFlu allows for precise antigen presentation, aiding in consistent immune responses across diverse populations. The use of nanoparticles in NanoFlu supports both a strong humoral and cell-mediated immune response, making it a promising candidate for seasonal influenza vaccination, especially among populations vulnerable to influenza-related complications (Woodson & Jha, 2023).

6.7.3. SpFN (Spike Ferritin Nanoparticle) COVID-19 Vaccine

The SpFN (Spike Ferritin Nanoparticle) COVID-19 Vaccine is an innovative vaccine candidate that uses ferritin nanoparticles to present the SARS-CoV-2 spike protein, potentially offering broad protection against COVID-19 and related coronaviruses. This vaccine platform is unique because it displays multiple spike protein trimers on a single ferritin nanoparticle, which enhances immunogenicity by providing a highly organized and multivalent antigen presentation to the immune system (Johnston et al., 2022).

Preclinical studies in nonhuman primates demonstrated that SpFN, when paired with an adjuvant (such as ALFQ), generated robust immune responses, including neutralizing antibodies and polyfunctional T-cell activity. This immune profile suggests potential efficacy not only against the primary SARS-CoV-2 strain but also against variants and other coronaviruses (Carmen et al., 2021). The structure of ferritin enables multiple copies of the spike protein to be displayed, enhancing antibody responses and providing a platform that could be adaptable for other viral threats.

Ferritin-based vaccines like SpFN are advantageous due to their stability and potential cross-reactivity, positioning them as a promising option for next-generation vaccines aimed at preventing not only SARS-CoV-2 infections but also future coronavirus pandemics (Joyce et al., 2021).

6.7.4. RTS,S/AS01 (Mosquirix) Malaria Vaccine

The RTS,S/AS01 (Mosquirix) Malaria Vaccine is the first malaria vaccine to receive approval for use, aimed at protecting

children in areas with high malaria prevalence. Developed by GlaxoSmithKline (GSK), Mosquirix® targets *Plasmodium falciparum*, the most deadly malaria parasite, and includes a recombinant protein from the parasite's circumsporozoite protein (CSP), which is assembled into a nanoparticle structure to enhance immunogenicity. The vaccine uses the AS01 adjuvant, a proprietary GSK adjuvant containing monophosphoryl lipid A and QS-21, which stimulates a strong immune response by activating both cellular and humoral immunity (Nadeem et al., 2022).

Clinical trials demonstrated the vaccine's efficacy in reducing malaria cases in young children, providing partial protection and reducing the severity of infections in regions with high transmission rates (Genito et al., 2023). Despite its moderate efficacy, Mosquirix® represents a significant step in malaria control efforts, particularly for vulnerable populations with limited access to other preventive measures. The success of RTS,S/AS01 has set a foundation for developing next-generation malaria vaccines that may offer broader protection and improved efficacy (Locke et al., 2024).

7. CHALLENGES and RISKS of NANOMATERIALS in MEDICINE

While nanomaterials offer tremendous potential in medical applications such as drug delivery, diagnostics, and vaccines, their use also comes with several challenges and risks that need to be carefully addressed. These challenges pertain to safety, manufacturing, regulatory concerns, and potential environmental impacts. Understanding and mitigating these risks is crucial for the successful development and deployment of nanomaterial-based therapies and diagnostics.

7.1. Safety and Toxicity Concerns

One of the most significant concerns with the use of nanomaterials in medicine is their potential toxicity. Nanoparticles behave differently from bulk materials due to their small size, high surface area, and unique physical and chemical properties, which can lead to unexpected interactions with biological systems. For example, nanoparticles can penetrate biological barriers like the blood-brain barrier or cell membranes, which larger particles cannot. This ability can result in unintended accumulation in organs such as the liver, lungs, kidneys, or spleen, potentially causing toxicity (Manke et al., 2013). The small size of nanoparticles also means they can be inhaled, absorbed through the skin, or ingested, potentially leading to systemic exposure (Khanna et al., 2015).

Certain nanomaterials, especially metal-based nanoparticles like silver or titanium dioxide, can generate reactive oxygen species (ROS) that lead to oxidative stress and inflammation in tissues. This oxidative stress can damage cells, DNA, and proteins, potentially leading to long-term health effects such as carcinogenesis or organ damage (R. K. Pandey & Prajapati, 2018). Furthermore, nanoparticles may elicit unintended immune responses, as they can activate immune cells, causing inflammation or allergic reactions. Some nanoparticles, on the other hand, might suppress immune responses, leading to immune evasion or reduced effectiveness of vaccines or therapies (Miethling-Graff et al., 2014).

Table 3: Vaccines incorporates nanoparticles

Vaccine Name	Nanomaterial	Mechanism	Advantages	references
Novavax COVID-19 Vaccine (NVX-CoV2373)	Protein nanoparticle (recombinant spike protein)	Protein nanoparticle displays spike proteins with Matrix-M™ adjuvant enhancing immune response	High immune response with easier storage compared to mRNA vaccines	(Lundstrom, 2023; Malabadi et al., 2021; Yadav et al., 2023).
NanoFluA® (Influenza Vaccine)	Protein nanoparticles (recombinant hemagglutinin nanoparticle)	Recombinant hemagglutinin proteins presented on nanoparticle platform to boost immune response	Strong, broad protection against antigenically drifted influenza strains	(Khalaj-Hedayati et al., 2020; Sia et al., 2021; Woodson & Jha, 2023).
SpFN (Spike Ferritin Nanoparticle COVID-19 Vaccine)	Ferritin nanoparticles	Ferritin nanoparticles display SARS-CoV-2 spike proteins in an organized structure	Strong immune response with potential for pan-coronavirus protection	(Carmen et al., 2021; Johnston et al., 2022; Joyce et al., 2021).
RTS,S/AS01 (Mosquirix® - Malaria Vaccine)	Lipid-based nanoparticle adjuvant (AS01)	Targets malaria circumsporozoite protein with lipid-based adjuvant enhancing immune response	Improved immunity in children, effective protection against malaria	(Genito et al., 2023; Locke et al., 2024; Nadeem et al., 2022)

7.2. Biodegradability and Long-Term Persistence

Many nanoparticles, particularly those made from metals or non-biodegradable polymers, may not break down easily in the body, raising concerns about long-term accumulation and potential toxicity. Metal-based nanoparticles, such as those composed of gold, silver, or quantum dots, can persist in the body due to their poor biodegradability. Over time, these nanoparticles may accumulate in organs and tissues, potentially leading to chronic toxicity or organ dysfunction (Bellanthurada et al., 2023). Ensuring biocompatibility is crucial for mitigating these risks. Biodegradable materials like lipid-based nanoparticles, PLGA (poly-lactic-co-glycolic acid), and protein-based nanoparticles are being developed to offer safer alternatives. However, even with biodegradable materials, the potential for incomplete degradation and residual effects remains a concern (Sathish Sundar et al., 2016).

Some non-biodegradable nanoparticles, particularly metal-based options, pose challenges for long-term health due to their persistence in the body. This necessitates ongoing research into safer nanomaterials and more comprehensive understanding of biocompatibility in clinical contexts (Paris et al., 2019).

7.3. Challenges in Manufacturing and Scalability

Producing nanomaterials for medical applications on a large scale, while maintaining quality and consistency, presents significant challenges. Nanomaterial production is complex and requires precise control over size, shape, and surface characteristics. Ensuring reproducibility is critical, as even small variations in particle size, surface charge, or morphology can significantly impact how nanoparticles interact with biological systems, affecting their biodistribution, toxicity, and efficacy (Operti et al., 2021). Consistency in quality control from batch to batch is essential for the safety and effectiveness of nanomedicines (Kaur et al., 2014).

The cost and scalability of nanomaterial production also present challenges. Nanomaterials are often expensive to produce due to specialized techniques like high-energy milling, vapor deposition, or complex chemical synthesis (Colombo et al., 2018). Scaling up these processes while maintaining cost-efficiency and quality remains a barrier to widespread adoption in medical applications.

Additionally, surface modification of nanoparticles, such as functionalization with ligands or stabilizing agents, is often necessary to improve biocompatibility and efficacy. This requirement adds complexity and cost to the manufacturing process, further complicating scalability (D. M. Patel et al., 2021). Ensuring that these surface modifications are consistently applied and effective across production batches remains a technical challenge.

7.4. Regulatory and Approval Challenges

The regulatory landscape for nanomaterials in medicine is still evolving. Regulatory bodies like the FDA and EMA are actively working to develop guidelines that ensure the safety and efficacy of nanotechnology-based products. However, the unique properties of nanomaterials create challenges for traditional regulatory frameworks. Traditional regulatory pathways for drugs and medical devices may not fully apply to nanomedicines. Nanoparticles behave differently due to their unique size, surface properties, and bio-distribution, which often require new testing methods and safety assessments (Bobo et al., 2016; Parveen et al., 2012). Consequently, it remains unclear how to apply existing guidelines to these materials, which can slow the approval process for nanomaterial-based therapeutics and diagnostics.

Additionally, there is currently no universal standard for characterizing nanomaterials regarding their physical, chemical, and biological properties. This lack of standardization complicates the comparison of results across different studies or regulatory submissions, leading to inconsistencies in evaluating safety and efficacy. Standardized methods for toxicity testing, particle characterization, and bio-distribution are urgently needed to streamline regulatory submissions and ensure safe, consistent outcomes (Ali et al., 2023; Foulkes et al., 2020).

7.5. Environmental and Ethical Concerns

Nanomaterials, once used in medicine or research, may end up in the environment, potentially leading to unforeseen ecological effects. Additionally, ethical concerns have emerged regarding their use in human trials and the long-term impacts of nanomaterials. Nanoparticles used in medical applications may eventually enter wastewater, soil, and ecosystems after being excreted from the human body or through the disposal of medical waste (V. Shah & Belozerovala, 2009). For instance, silver and titanium dioxide nanoparticles, widely used in consumer products, have been shown to negatively impact aquatic life, plants, and microorganisms, highlighting the potential environmental risks (Dakal et al., 2016). The long-term ecological consequences of extensive nanoparticle use, particularly in relation to their persistence in the environment, remain uncertain and require further investigation.

The ethical implications of introducing new, untested nanomaterials into humans are also a significant concern. Comprehensive safety data must be collected from preclinical studies to ensure that human trials do not expose participants to unforeseen risks. Balancing the drive for innovation in nanomedicine with ensuring participant safety is essential, particularly when vulnerable populations or high-risk conditions are involved (Fadeel & Garcia-Bennett, 2010). Ethical considerations are central to the responsible advancement of nanomedicine, as they ensure both safety and respect for participants involved in clinical research.

7.6. Nanoparticle Stability and Storage

Nanomaterials, especially those used in vaccines and drug delivery systems, face significant stability challenges during storage and transportation, which can impact their efficacy and safety. For instance, lipid-based and polymeric nanoparticles can degrade over time, resulting in reduced potency or altered behavior in the body. Factors such as temperature, light exposure, and pH significantly impact the stability of these nanomaterials during storage (Crommelin et al., 2021; Kis, 2022). The shelf life of these nanoparticles is critical in ensuring they maintain their intended effects once administered.

In particular, many nanomaterial-based vaccines, such as lipid nanoparticles used in mRNA vaccines, require ultra-low temperature storage, posing logistical challenges in distribution. Maintaining a cold chain, typically at temperatures below -20°C, is essential for preserving the stability of these sensitive materials. This requirement can be especially problematic in regions lacking refrigeration infrastructure. Research is ongoing to improve the thermal stability of nanoparticles, aiming to allow storage at more standard temperatures without compromising effectiveness (Schoenmaker et al., 2021).

8. FUTURE DIRECTIONS for NANOMATERIALS in MEDICINE

The future of nanomaterials in medicine holds significant promise across fields like drug delivery, diagnostics, regenerative medicine, and vaccines. Researchers are making strides in developing new nanomaterials, optimizing existing technologies, and addressing limitations to improve patient care. Personalized medicine is a key area where nanomaterials are expected to excel, particularly with patient-specific drug delivery systems that target genetic profiles and disease characteristics. These advancements are anticipated to make treatments more effective while reducing side effects by customizing therapy to individual biology (Mitravotri et al., 2015). Nanomaterials are also enhancing biomarker-based diagnostics, which may enable real-time monitoring of disease progression and dynamic adjustment of treatments (Pelaz et al., 2017).

Further advancements include the development of smart, responsive nanomaterials capable of reacting to environmental cues, such as pH or temperature, allowing for precision in treatment delivery. For example, stimuli-responsive nanoparticles are being designed to release drugs selectively in diseased tissues, reducing off-target effects and increasing efficacy. This is especially valuable in cancer therapy, where multifunctional nanoparticles could deliver a combination of

treatments like chemotherapy, immunotherapy, and gene therapy within a single platform (A. Z. Wang et al., 2012). Theranostic nanoparticles, which combine therapeutic and diagnostic functions, are another emerging trend, offering the ability to both treat and monitor diseases like cancer simultaneously (C. Zhang et al., 2020).

Regenerative medicine is another field set to benefit from nanotechnology. Nanomaterials in neurotherapeutics, particularly nanoparticles that can cross the blood-brain barrier, promise new treatments for neurological disorders, and scaffold-based nanofiber technologies are advancing tissue engineering by promoting neural and other tissue regeneration (Lowe et al., 2019). In addition, the combination of nanotechnology with 3D bioprinting could enable patient-specific tissue engineering, reducing the need for donor organs and accelerating recovery. Regulatory challenges remain, as the unique properties of nanomaterials require the adaptation of regulatory frameworks to ensure safe clinical translation. Standardized guidelines for evaluating nanomaterials' safety, efficacy, and long-term effects are crucial to balance innovation with patient safety (Domb et al., 2021).

9. CONCLUSION

Nanomaterials have emerged as a transformative force in modern medicine, offering revolutionary solutions across a broad range of applications including drug delivery, diagnostics, vaccines, and regenerative medicine. Their unique physical, chemical, and biological properties enable highly targeted, efficient, and customizable therapies, which are particularly valuable in the treatment of complex diseases such as cancer, neurological disorders, and infectious diseases.

From the early successes of nanoparticle-based drug delivery systems like Doxil and Abraxane to the recent breakthroughs in mRNA vaccines enabled by lipid nanoparticles, nanotechnology is demonstrating its ability to address critical challenges in healthcare. Nanomaterials are not only improving the effectiveness of treatments but also reducing side effects by ensuring precise targeting, controlled release, and enhanced biocompatibility.

However, as promising as nanotechnology is, its integration into mainstream medicine also faces challenges and risks. Issues related to toxicity, long-term safety, environmental impact, manufacturing scalability, and regulatory frameworks need to be carefully managed. Advances in developing biodegradable, biocompatible, and stimuli-responsive nanomaterials are already addressing many of these concerns, paving the way for safer and more effective nanomedicines.

The future directions of nanomedicine are incredibly exciting, with the potential for personalized therapies, smart nanomaterials, and theranostics that combine treatment and diagnostics into a single platform. Moreover, ongoing research into the role of nanomaterials in regenerative medicine, cancer treatment, and overcoming the blood-brain barrier promises to expand the possibilities of what nanotechnology can achieve in healthcare.

While there are challenges to overcome, the role of nanomaterials in medicine is set to grow significantly in the coming years. With continued innovation, improved safety protocols, and robust regulatory frameworks, nanotechnology will increasingly become a cornerstone of future medical advances, offering new hope for treating diseases more effectively and improving patient outcomes globally.

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References

- Abd El-Aziz, A. M., Abd El-Fattah, A., El-Maghraby, A., Ghareeb, D. A., and Kandil, S. (2021). Viscoelasticity, Mechanical Properties, and In Vitro Bioactivity of Gelatin/Borosilicate Bioactive Glass Nanocomposite Hydrogels as Potential Scaffolds for Bone Regeneration. *Polymers*, **13**(12), 2014. <https://doi.org/10.3390/polym13122014>
- Abdellatif, A. A. H., Younis, M. A., Alsharidah, M., Al Rugaie, O., and Tawfeek, H. M. (2022). Biomedical Applications of Quantum Dots: Overview, Challenges, and Clinical Potential. *International Journal of Nanomedicine*, **17**, 1951–1970. <https://doi.org/10.2147/IJN.S357980>
- Abdou, S. M., Moustafa, A., and Allam, N. K. (2024). Patterned PCL/PGS Nanofibrous Hyaluronic Acid-Coated Scaffolds Promote Cellular Response and Modulate Gene Expression Profiles. *ACS Applied Bio Materials*, **7**(4), 2569–2581. <https://doi.org/10.1021/acsabm.4c00196>
- Adepu, S., and Ramakrishna, S. (2021). Controlled Drug Delivery Systems: Current Status and Future Directions. *Molecules (Basel, Switzerland)*, **26**(19), 5905. <https://doi.org/10.3390/molecules26195905>
- Ahmad, A., Khan, F., Mishra, R. K., and Khan, R. (2019). Precision cancer nanotherapy: evolving role of multifunctional nanoparticles for cancer active targeting. *Journal of Medicinal Chemistry*, **62**(23), 10475–10496. <https://doi.org/10.1021/acs.jmedchem.9b00511>
- Ahmed, M., Kurungottu, P., Swetha, K., Atla, S., Ashok, N., Nagamalleswari, E., Bonam, S. R., Sahu, B. D., and Kurapati, R. (2024). Role of NLRP3 inflammasome in nanoparticle adjuvant-mediated immune response. *Biomaterials Science*. <https://doi.org/10.1039/D4BM00439F>
- Ahsan, A., Thomas, N., Barnes, T. J., Subramaniam, S., Loh, T. C., Joyce, P., and Prestidge, C. A. (2024). Lipid Nanocarriers-Enabled Delivery of Antibiotics and Antimicrobial Adjuvants to Overcome Bacterial Biofilms. *Pharmaceutics*, **16**(3), 396. <https://doi.org/10.3390/pharmaceutics16030396>
- Akombaetwa, N., Bwanga, A., Makoni, P. A., and Witika, B. A. (2022). Applications of electrospun drug-eluting nanofibers in wound healing: Current and future perspectives. *Polymers*, **14**(14), 2931. <https://doi.org/10.3390/polym14142931>
- Alam, N., Tong, L., He, Z., Tang, R., Ahsan, L., and Ni, Y. (2023). Mechanically Compressed Barriers Improve Paper-Based Lateral Flow Assay Sensitivity for COVID-19 Nucleic Acid Detection. *Industrial & Engineering Chemistry Research*, **62**(44), 18800–18809. <https://doi.org/10.1021/acs.iecr.3c02828>
- Aldughaim, M. S., Muthana, M., Alsaffar, F., and Barker, M. D. (2020). Specific Targeting of PEGylated Liposomal Doxorubicin (Doxil®) to Tumour Cells Using a Novel TIMP3 Peptide. *Molecules*, **26**(1), 100. <https://doi.org/10.3390/molecules26010100>
- Alfayez, M., Kantarjian, H., Kadia, T., Ravandi-Kashani, F., and Daver, N. (2020). CPX-351 (vyxeos) in AML. *Leukemia & Lymphoma*, **61**(2), 288–297. <https://doi.org/10.1080/10428194.2019.1660970>
- Alghamdi, M. A., Fallica, A. N., Virzi, N., Kesharwani, P., Pittalà, V., and Greish, K. (2022). The Promise of Nanotechnology in Personalized Medicine. *Journal of Personalized Medicine*, **12**(5), 673. <https://doi.org/10.3390/jpm12050673>
- Alghamdi, M. F., and Redwan, E. M. (2021). Advances in the diagnosis of autoimmune diseases based on citrullinated peptides/proteins. *Expert Review of Molecular Diagnostics*, **21**(7), 685–702. <https://doi.org/10.1080/14737159.2021.1933946>
- Ali, F., Neha, K., and Parveen, S. (2023). Current regulatory landscape of nanomaterials and nanomedicines: A global

- perspective. *Journal of Drug Delivery Science and Technology*, **80**, 104118. <https://doi.org/https://doi.org/10.1016/j.jddst.2022.104118>
- Allahyari, M., and Mohit, E. (2016). Peptide/protein vaccine delivery system based on PLGA particles. *Human Vaccines & Immunotherapeutics*, **12**(3), 806–828.
- Almatroudi, A. (2024). Unlocking the Potential of Silver Nanoparticles: From Synthesis to Versatile Bio-Applications. *Pharmaceutics*, **16**(9), 1232. <https://doi.org/10.3390/pharmaceutics16091232>
- Andryukov, B. G. (2020). Six decades of lateral flow immunoassay: from determining metabolic markers to diagnosing COVID-19. *AIMS Microbiology*, **6**(3), 280–304. <https://doi.org/10.3934/microbiol.2020018>
- Asleh, R., Vucicevic, D., Petterson, T. M., Kremers, W. K., Pereira, N. L., Daly, R. C., Edwards, B. S., Steidley, D. E., Scott, R. L., and Kushwaha, S. S. (2022). Sirolimus-Based Immunosuppression Is Associated with Decreased Incidence of Post-Transplant Lymphoproliferative Disorder after Heart Transplantation: A Double-Center Study. *Journal of Clinical Medicine*, **11**(2), 322. <https://doi.org/10.3390/jcm11020322>
- Augustine, J. J., Bodziak, K. A., and Hricik, D. E. (2007). Use of sirolimus in solid organ transplantation. *Drugs*, **67**(3), 369–391. <https://doi.org/10.2165/00003495-200767030-00004>
- Bai, X., Smith, Z. L., Wang, Y., Butterworth, S., and Tirella, A. (2022). Sustained Drug Release from Smart Nanoparticles in Cancer Therapy: A Comprehensive Review. *Micromachines*, **13**(10), 1623. <https://doi.org/10.3390/mi13101623>
- Bejarano, J., Navarro-Marquez, M., Morales-Zavala, F., Morales, J. O., Garcia-Carvajal, I., Araya-Fuentes, E., Flores, Y., Verdejo, H. E., Castro, P. F., Lavandero, S., and Kogan, M. J. (2018). Nanoparticles for diagnosis and therapy of atherosclerosis and myocardial infarction: evolution toward prospective theranostic approaches. *Theranostics*, **8**(17), 4710–4732. <https://doi.org/10.7150/thno.26284>
- Bellanthudawa, B. K. A., Nawalage, N. M. S. K., Handapangoda, H. M. A. K., Suvendran, S., Wijayasenarathne, K. A. S. H., Rathnasuriya, M. L. D., Wickramasinghe, P. G. M. U., Aberathna, A. A. A. U., Tennakoon, A., and Perera, I. J. J. U. N. (2023). A perspective on biodegradable and non-biodegradable nanoparticles in industrial sectors: applications, challenges, and future prospects. *Nanotechnology for Environmental Engineering*, **8**(4), 975–1013. <https://doi.org/10.1007/s41204-023-00344-7>
- Bellotti, E., Cascone, M. G., Barbani, N., Rossin, D., Rastaldo, R., Giachino, C., and Cristallini, C. (2021). Targeting Cancer Cells Overexpressing Folate Receptors with New Terpolymer-Based Nanocapsules: Toward a Novel Targeted DNA Delivery System for Cancer Therapy. *Biomedicines*, **9**(9), 1275. <https://doi.org/10.3390/biomedicines9091275>
- Benesch, M., and Urban, C. (2008). Liposomal cytarabine for leukemic and lymphomatous meningitis: recent developments. *Expert Opinion on Pharmacotherapy*, **9**(2), 301–309. <https://doi.org/10.1517/14656566.9.2.301>
- Berkoldt, M., Mutschlechner, W., and Orth-Höller, D. (2017). Comparison of rapid hybridization-based pathogen identification and resistance evaluation in sepsis using the Verigene® device paired with “good old culture.” *Wiener Klinische Wochenschrift*, **129**(11), 435–441. <https://doi.org/10.1007/s00508-016-1057-y>
- Bober, Z., Bartusik-Aebisher, D., and Aebisher, D. (2022). Application of Dendrimers in Anticancer Diagnostics and Therapy. *Molecules*, **27**(10), 3237. <https://doi.org/10.3390/molecules27103237>
- Bobo, D., Robinson, K. J., Islam, J., Thurecht, K. J., and Corrie, S. R. (2016). Nanoparticle-Based Medicines: A Review of FDA-Approved Materials and Clinical Trials to Date. *Pharmaceutical Research*, **33**(10), 2373–2387. <https://doi.org/10.1007/s11095-016-1958-5>
- Boriachek, K., Islam, M. N., Möller, A., Salomon, C., Nguyen, N.-T., Hossain, M. S. A., Yamauchi, Y., and Shiddiky, M. J. A. (2018). Biological Functions and Current Advances in Isolation and Detection Strategies for Exosome Nanovesicles. *Small*, **14**(6), 1702153. <https://doi.org/https://doi.org/10.1002/smll.201702153>
- Bose, A., Roy Burman, D., Sikdar, B., and Patra, P. (2021). Nanomicelles: Types, properties and applications in drug delivery. *IET Nanobiotechnology*, **15**(1), 19–27. <https://doi.org/10.1049/nbt2.12018>
- Bravo-Vázquez, L. A., Méndez-García, A., Rodríguez, A. L., Sahare, P., Pathak, S., Banerjee, A., Duttaroy, A. K., and Paul, S. (2023). Applications of nanotechnologies for miRNA-based cancer therapeutics: current advances and future perspectives. *Frontiers in Bioengineering and Biotechnology*, **11**, 1208547. <https://doi.org/10.3389/fbioe.2023.1208547>
- Buño, A., Oliver, P., Fernández Calle, P., Alcaide, M. J., Gómez Rioja, R., Iturzaeta, J. M., and Mateos, F. (2008). Blood Gases, Electrolytes and Metabolites Point-of-Care Testing at La Paz University Hospital. *Point of Care*, **7**(3), 146. <https://doi.org/10.1097/01.POC.0000335853.78014.80>
- Carabineiro, S. A. C. (2017). Applications of gold nanoparticles in nanomedicine: recent advances in vaccines. *Molecules*, **22**(5), 857. <https://doi.org/10.3390/molecules22050857>
- Carmen, J. M., Shrivastava, S., Lu, Z., Anderson, A., Morrison, E. B., Sankhala, R. S., Chen, W.-H., Chang, W. C., Bolton, J. S., Matyas, G. R., Michael, N. L., Joyce, M. G., Modjarrad, K., Currier, J. R., Bergmann-Leitner, E., Malloy, A. M. W., and Rao, M. (2021). SARS-CoV-2 ferritin nanoparticle vaccine induces robust innate immune activity driving polyfunctional spike-specific T cell responses. *Npj Vaccines*, **6**(1), 151. <https://doi.org/10.1038/s41541-021-00414-4>
- Cellini, A., Pedna, M. F., Del Bianco, F., and Sambri, V. (2015). Evaluation of the Verigene® Blood Culture Nucleic Acid test for rapid identification of gram positive pathogens from positive blood cultures. *Microbiologia Medica*, **30**(1). <https://doi.org/10.4081/mm.2015.4945>
- Chauhan, N., Chauhan, A., and Jain, S. (2024). *Advancements in Nanomedicine for Neurodegenerative Diseases: A Comprehensive Review*. <https://doi.org/10.22541/au.172983606.69080943/v1>
- Chehelgerdi, M., Chehelgerdi, M., Allela, O. Q. B., Pecho, R. D. C., Jayasankar, N., Rao, D. P., Thamaraiyani, T., Vasanthan, M., Viktor, P., Lakshmaiyi, N., Saadh, M. J., Amajd, A., Abo-Zaid, M. A., Castillo-Acoba, R. Y., Ismail, A. H., Amin, A. H., and Akhavan-Sigari, R. (2023). Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation. *Molecular Cancer*, **22**(1), 169. <https://doi.org/10.1186/s12943-023-01865-0>
- Chen, D., Monteiro-Riviere, N. A., and Zhang, L. W. (2017). Intracellular imaging of quantum dots, gold, and iron oxide nanoparticles with associated endocytic pathways. *Wiley Interdisciplinary Reviews. Nanomedicine and Nanobiotechnology*, **9**(2), e1419. <https://doi.org/10.1002/wnan.1419>
- Chen, Y., Dong, X., Shafiq, M., Myles, G., Radacs, N., and Mo, X. (2022). Recent advancements on three-dimensional electrospun nanofiber scaffolds for tissue engineering. *Advanced Fiber Materials*, **4**(5), 959–986. <https://doi.org/10.1016/j.pmatsci.2020.100721>
- Chis, A. A., Dobrea, C., Morgovan, C., Arseniu, A. M., Rus, L. L., Butuca, A., Juncan, A. M., Totan, M., Vonica-Tincu, A. L., and Cormos, G. (2020). Applications and limitations of dendrimers in biomedicine. *Molecules*, **25**(17), 3982. <https://doi.org/10.3390/molecules25173982>
- Choksi, A. U., Khan, A. I., Lokeshwar, S. D., Segal, D., Weiss, R. M., and Martin, D. T. (2022). Functionalized nanoparticles targeting biomarkers for prostate cancer

- imaging and therapy. *American Journal of Clinical and Experimental Urology*, **10**(3), 142–153.
- Chu, S., Shi, X., Tian, Y., and Gao, F. (2022). pH-Responsive Polymer Nanomaterials for Tumor Therapy. *Frontiers in Oncology*, **12**, 855019. <https://doi.org/10.3389/fonc.2022.855019>
- Colombo, S., Beck-Broichsitter, M., Bøtker, J. P., Malmsten, M., Rantanen, J., and Bohr, A. (2018). Transforming nanomedicine manufacturing toward Quality by Design and microfluidics. *Advanced Drug Delivery Reviews*, **128**, 115–131. <https://doi.org/https://doi.org/10.1016/j.addr.2018.04.004>
- Crommelin, D. J. A., Anchordoquy, T. J., Volkin, D. B., Jiskoot, W., and Mastrobattista, E. (2021). Addressing the Cold Reality of mRNA Vaccine Stability. *Journal of Pharmaceutical Sciences*, **110**(3), 997–1001. <https://doi.org/https://doi.org/10.1016/j.xphs.2020.12.006>
- Cui, J., Qin, S., Zhou, Y., Zhang, S., Sun, X., Zhang, M., Cui, J., Fang, W., Gu, K., Li, Z., Wang, J., Chen, X., Yao, J., Zhou, J., Wang, G., Bai, Y., Xiao, J., Qiu, W., Wang, B., ... Wang, L. (2024). Irinotecan hydrochloride liposome HR070803 in combination with 5-fluorouracil and leucovorin in locally advanced or metastatic pancreatic ductal adenocarcinoma following prior gemcitabine-based therapy (PAN-HEROIC-1): a phase 3 trial. *Signal Transduction and Targeted Therapy*, **9**(1), 248. <https://doi.org/10.1038/s41392-024-01948-4>
- Dakal, T. C., Kumar, A., Majumdar, R. S., and Yadav, V. (2016). Mechanistic basis of antimicrobial actions of silver nanoparticles. *Frontiers in Microbiology*, **7**, 1831. <https://doi.org/10.3389/fmicb.2016.01831>
- Dam, P., Celik, M., Ustun, M., Saha, S., Saha, C., Kacar, E. A., Kugu, S., Karagulle, E. N., Tasoglu, S., Buyukserin, F., Mondal, R., Roy, P., Macedo, M. L. R., Franco, O. L., Cardoso, M. H., Altuntas, S., and Mandal, A. K. (2023). Wound healing strategies based on nanoparticles incorporated in hydrogel wound patches. *RSC Advances*, **13**(31), 21345–21364. <https://doi.org/10.1039/d3ra03477a>
- Dastgheib, Z. S., Abolmaali, S. S., Farahavar, G., Salmanpour, M., and Tamaddon, A. M. (2024). Gold nanostructures in melanoma: Advances in treatment, diagnosis, and theranostic applications. *Heliyon*, **10**(15). <https://doi.org/10.1016/j.heliyon.2024.e35655>
- Date, A. A., Hanes, J., and Ensign, L. M. (2016). Nanoparticles for oral delivery: Design, evaluation and state-of-the-art. *Journal of Controlled Release: Official Journal of the Controlled Release Society*, **240**, 504–526. <https://doi.org/10.1016/j.jconrel.2016.06.016>
- De Angelis, G., Posteraro, B., De Carolis, E., Menchinelli, G., Franceschi, F., Tumbarello, M., De Pascale, G., Spanu, T., and Sanguinetti, M. (2018). T2Bacteria magnetic resonance assay for the rapid detection of ESKAPEc pathogens directly in whole blood. *Journal of Antimicrobial Chemotherapy*, **73**(suppl_4), iv20–iv26. <https://doi.org/10.1093/jac/dky049>
- Dewey, H. M., Lamb, A., and Budhathoki-Uprety, J. (2024). Recent advances on applications of single-walled carbon nanotubes as cutting-edge optical nanosensors for biosensing technologies. *Nanoscale*, **16**, 16344. <https://doi.org/10.1039/D4NR01892C>
- Dheyab, M. A., Aziz, A. A., Khaniabadi, P. M., Jameel, M. S., Oladzadabbasabadi, N., Rahman, A. A., Braim, F. S., and Mehrdel, B. (2023). Gold nanoparticles-based photothermal therapy for breast cancer. *Photodiagnosis and Photodynamic Therapy*, **42**, 103312. <https://doi.org/10.1016/j.pdpdt.2023.103312>
- Dicko, A., Kwak, S., Frazier, A. A., Mayer, L. D., and Liboiron, B. D. (2010). Biophysical characterization of a liposomal formulation of cytarabine and daunorubicin. *International Journal of Pharmaceutics*, **391**(1), 248–259. <https://doi.org/https://doi.org/10.1016/j.ijpharm.2010.02.014>
- Dilmani, S. A., Koç, S., Erkut, T. S., and Gümüşderelioğlu, M. (2024). Polymer-clay nanofibrous wound dressing materials containing different boron compounds. *Journal of Trace Elements in Medicine and Biology*, **83**, 127408. <https://doi.org/https://doi.org/10.1016/j.jtemb.2024.127408>
- Dimitriou, N. M., Tsekenis, G., Balanikas, E. C., Pavlopoulou, A., Mitsiogianni, M., Mantso, T., Pashos, G., Boudouvis, A. G., Lykakis, I. N., Tsigaridas, G., Panayiotidis, M. I., Yannopapas, V., and Georgakilas, A. G. (2017). Gold nanoparticles, radiations and the immune system: Current insights into the physical mechanisms and the biological interactions of this new alliance towards cancer therapy. *Pharmacology & Therapeutics*, **178**, 1–17. <https://doi.org/https://doi.org/10.1016/j.pharmthera.2017.03.006>
- Dinh, L., Mahon, L., and Yan, B. (2024). Nano-Encapsulation and Conjugation Applied in the Development of Lipid Nanoparticles Delivering Nucleic Acid Materials to Enable Gene Therapies. *Applied Nano*, **5**(3), 143–161. <https://doi.org/10.3390/applnano5030011>
- Domb, A. J., Sharifzadeh, G., Nahum, V., and Hosseinkhani, H. (2021). Safety Evaluation of Nanotechnology Products. *Pharmaceutics*, **13**(10), 1615. <https://doi.org/10.3390/pharmaceutics13101615>
- Domínguez, A. R., Hidalgo, D. O., Garrido, R. V., and Sánchez, E. T. (2005). Liposomal cytarabine (DepoCyt®) for the treatment of neoplastic meningitis. *Clinical and Translational Oncology*, **7**(6), 232–238. <https://doi.org/10.1007/BF02710168>
- Dorta-Gorrín, A., Navas-Méndez, J., Gozalo-Margüello, M., Miralles, L., and García-Hevia, L. (2023). Detection of SARS-CoV-2 Based on Nucleic Acid Amplification Tests (NAATs) and Its Integration into Nanomedicine and Microfluidic Devices as Point-of-Care Testing (POCT). *International Journal of Molecular Sciences*, **24**(12), 10233. <https://doi.org/10.3390/ijms241210233>
- Duggan, S. T., and Keating, G. M. (2011). Pegylated liposomal doxorubicin: a review of its use in metastatic breast cancer, ovarian cancer, multiple myeloma and AIDS-related Kaposi's sarcoma. *Drugs*, **71**(18), 2531–2558. <https://doi.org/10.2165/11207510-000000000-00000>
- Dulińska-Litewka, J., Łazarczyk, A., Hałubiec, P., Szafranski, O., Karnas, K., and Karewicz, A. (2019). Superparamagnetic Iron Oxide Nanoparticles-Current and Prospective Medical Applications. *Materials*, **12**(4), 617. <https://doi.org/10.3390/ma12040617>
- Dykman, L. A. (2020). Gold nanoparticles for preparation of antibodies and vaccines against infectious diseases. *Expert Review of Vaccines*, **19**(5), 465–477. <https://doi.org/10.1080/14760584.2020.1758070>
- Elmowafy, M., and Al-Sanea, M. M. (2021). Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. *Saudi Pharmaceutical Journal*, **29**(9), 999–1012. <https://doi.org/10.1016/j.jsps.2021.07.015>
- Elmowafy, M., Shalaby, K., Elkomy, M. H., Alsaidan, O. A., Gomaa, H. A. M., Abdelgawad, M. A., and Mostafa, E. M. (2023). Polymeric Nanoparticles for Delivery of Natural Bioactive Agents: Recent Advances and Challenges. *Polymers*, **15**(5), 1123. <https://doi.org/10.3390/polym15051123>
- Fadeel, B., and Garcia-Bennett, A. E. (2010). Better safe than sorry: Understanding the toxicological properties of inorganic nanoparticles manufactured for biomedical applications. *Advanced Drug Delivery Reviews*, **62**(3), 362–374. <https://doi.org/https://doi.org/10.1016/j.addr.2009.11.008>
- Foulkes, R., Man, E., Thind, J., Yeung, S., Joy, A., and Hoskins, C. (2020). The regulation of nanomaterials and nanomedicines for clinical application: current and future perspectives. *Biomaterials Science*, **8**(17), 4653–4664. <https://doi.org/10.1039/D0BM00558D>
- Gagliardi, A., Giuliano, E., Venkateswararao, E., Fresta, M.,

- Bulotta, S., Awasthi, V., and Cosco, D. (2021). Biodegradable Polymeric Nanoparticles for Drug Delivery to Solid Tumors. *Frontiers in Pharmacology*, **12**, 601626. <https://doi.org/10.3389/fphar.2021.601626>
- Genchi, G., Lauria, G., Catalano, A., Carocci, A., and Sinicropi, M. S. (2024). Neuroprotective Effects of Curcumin in Neurodegenerative Diseases. *Foods*, **13**(11), 1774. <https://doi.org/10.3390/foods13111774>
- Genito, C. J., Brooks, K., Smith, A., Ryan, E., Soto, K., Li, Y., Warter, L., and Dutta, S. (2023). Protective antibody threshold of RTS,S/AS01 malaria vaccine correlates antigen and adjuvant dose in mouse model. *Npj Vaccines*, **8**(1), 114. <https://doi.org/10.1038/s41541-023-00714-x>
- Ghasemiyeh, P., and Mohammadi-Samani, S. (2018). Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages. *Research in Pharmaceutical Sciences*, **13**(4), 288–303. <https://doi.org/10.4103/1735-5362.235156>
- Gigliobianco, M. R., Casadidio, C., Censi, R., and Di Martino, P. (2018). Nanocrystals of Poorly Soluble Drugs: Drug Bioavailability and Physicochemical Stability. *Pharmaceutics*, **10**(3), 134. <https://doi.org/10.3390/pharmaceutics10030134>
- Gkartziou, F., Giormezis, N., Spiliopoulou, I., and Antimisiaris, S. G. (2021). Nanobiosystems for Antimicrobial Drug-Resistant Infections. *Nanomaterials*, **11**(5), 1075. <https://doi.org/10.3390/nano11051075>
- Gomes-da-Silva, L. C., Fonseca, N. A., Moura, V., Pedroso de Lima, M. C., Simões, S., and Moreira, J. N. (2012). Lipid-Based Nanoparticles for siRNA Delivery in Cancer Therapy: Paradigms and Challenges. *Accounts of Chemical Research*, **45**(7), 1163–1171. <https://doi.org/10.1021/ar300048p>
- Gong, J., Shi, T., Liu, J., Pei, Z., Liu, J., Ren, X., Li, F., and Qiu, F. (2023). Dual-drug codelivery nanosystems: An emerging approach for overcoming cancer multidrug resistance. *Biomedicine & Pharmacotherapy*, **161**, 114505. <https://doi.org/https://doi.org/10.1016/j.biopha.2023.114505>
- Graván, P., Aguilera-Garrido, A., Marchal, J. A., Navarro-Marchal, S. A., and Galisteo-González, F. (2023). Lipid-core nanoparticles: Classification, preparation methods, routes of administration and recent advances in cancer treatment. *Advances in Colloid and Interface Science*, **314**, 102871. <https://doi.org/https://doi.org/10.1016/j.cis.2023.102871>
- Guevara, M. L., Persano, F., and Persano, S. (2020). Advances in Lipid Nanoparticles for mRNA-Based Cancer Immunotherapy. *Frontiers in Chemistry*, **8**. <https://www.frontiersin.org/journals/chemistry/articles/10.3389/fchem.2020.589959>
- Haba, M. Ş, Şerban, D. N., Şerban, L., Tudorancea, I. M., Haba, R. M., Mitu, O., Iliescu, R., and Tudorancea, I. (2021). Nanomaterial-Based Drug Targeted Therapy for Cardiovascular Diseases: Ischemic Heart Failure and Atherosclerosis. *Crystals*, **11**(10), 1172. <https://doi.org/10.3390/cryst11101172>
- Haeri, A., Osouli, M., Bayat, F., Alavi, S., and Dadashzadeh, S. (2018). Nanomedicine approaches for sirolimus delivery: a review of pharmaceutical properties and preclinical studies. *Artificial Cells, Nanomedicine, and Biotechnology*, **46**(sup1), 1–14. <https://doi.org/10.1080/21691401.2017.1408123>
- Haider, M., Abdin, S. M., Kamal, L., and Orive, G. (2020). Nanostructured lipid carriers for delivery of chemotherapeutics: A review. *Pharmaceutics*, **12**(3), 288. <https://doi.org/10.3390/pharmaceutics12030288>
- Harrison, T. S., and Lyseng-Williamson, K. A. (2013). Vincristine Sulfate Liposome Injection. *BioDrugs*, **27**(1), 69–74. <https://doi.org/10.1007/s40259-012-0002-5>
- Herranz, F., Almarza, E., Rodríguez, I., Salinas, B., Rosell, Y., Desco, M., Bulte, J. W., and Ruiz-Cabello, J. (2011). The application of nanoparticles in gene therapy and magnetic resonance imaging. *Microscopy Research and Technique*, **74**(7), 577–591. <https://doi.org/10.1002/jemt.20992>
- Hersh, A. M., Alomari, S., and Tyler, B. M. (2022). Crossing the Blood-Brain Barrier: Advances in Nanoparticle Technology for Drug Delivery in Neuro-Oncology. *International Journal of Molecular Sciences*, **23**(8). <https://doi.org/10.3390/ijms23084153>
- Hlapisi, N., Songca, S. P., and Ajibade, P. A. (2024). Capped Plasmonic Gold and Silver Nanoparticles with Porphyrins for Potential Use as Anticancer Agents—A Review. *Pharmaceutics*, **16**(10), 1268. <https://doi.org/10.3390/pharmaceutics16101268>
- Hood, M. N., Blankholm, A. D., and Stolpen, A. (2019). The Rise of Off-Label Iron-Based Agents in Magnetic Resonance Imaging. *Journal of Radiology Nursing*, **38**(1), 38–41. <https://doi.org/https://doi.org/10.1016/j.jradnu.2018.11.004>
- Hraber, P., Bradfute, S., Clarke, E., Ye, C., and Pitard, B. (2018). Amphiphilic block copolymer delivery of a DNA vaccine against Zika virus. *Vaccine*, **36**(46), 6911–6917. <https://doi.org/https://doi.org/10.1016/j.vaccine.2018.10.022>
- Huang, S., and Huang, G. (2024). The utilization of quantum dot labeling as a burgeoning technique in the field of biological imaging. *RSC Advances*, **14**(29), 20884–20897. <https://doi.org/10.1039/d4ra04402a>
- Huang, T., Peng, L., Han, Y., Wang, D., He, X., Wang, J., and Ou, C. (2022). Lipid nanoparticle-based mRNA vaccines in cancers: Current advances and future prospects. *Frontiers in Immunology*, **13**. <https://www.frontiersin.org/journals/immunology/article/10.3389/fimmu.2022.922301>
- Huda, M. N., Nafiujjaman, M., Deaguero, I. G., Okonkwo, J., Hill, M. L., Kim, T., and Nurunnabi, M. (2021). Potential Use of Exosomes as Diagnostic Biomarkers and in Targeted Drug Delivery: Progress in Clinical and Preclinical Applications. *ACS Biomaterials Science & Engineering*, **7**(6), 2106–2149. <https://doi.org/10.1021/acsbiomaterials.1c00217>
- Ibrahim, M., Abuwatfa, W. H., Awad, N. S., Sabouni, R., and Hussein, G. A. (2022). Encapsulation, Release, and Cytotoxicity of Doxorubicin Loaded in Liposomes, Micelles, and Metal-Organic Frameworks: A Review. *Pharmaceutics*, **14**(2), 254. <https://doi.org/10.3390/pharmaceutics14020254>
- Islam, M. A., Hasan, M., Rahman, M., Mobarak, M. H., Mimona, M. A., and Hossain, N. (2024). Advances and significances of carbon nanotube applications: A comprehensive review. *European Polymer Journal*, **220**, 113443. <https://doi.org/10.1016/j.eurpolymj.2024.113443>
- Jaeckle, K. A., Batchelor, T., O'Day, S. J., Phuphanich, S., New, P., Lesser, G., Cohn, A., Gilbert, M., Aiken, R., Heros, D., Rogers, L., Wong, E., Fulton, D., Gutheil, J. C., Baidas, S., Kennedy, J. M., Mason, W., Moots, P., Russell, C., ... Howell, S. B. (2002). An Open Label Trial of Sustained-release Cytarabine (DepoCyt™) for the Intrathecal Treatment of Solid Tumor Neoplastic Meningitis. *Journal of Neuro-Oncology*, **57**(3), 231–239. <https://doi.org/10.1023/A:1015752331041>
- Janib, S. M., Moses, A. S., and MacKay, J. A. (2010). Imaging and drug delivery using theranostic nanoparticles. *Advanced Drug Delivery Reviews*, **62**(11), 1052–1063. <https://doi.org/10.1016/j.addr.2010.08.004>
- Javed, Y., Hussain, M. I., Yaseen, M., and Asif, M. (2019). Gold-Iron Oxide Nanohybrids: Characterization and Biomedical Applications. In *Hybrid Nanocomposites*. Jenny Stanford Publishing. <https://doi.org/10.1201/9780429000966>
- Jha, A., and Pathak, Y. (2022). Chapter 6 - Polymeric nanomaterials for infectious diseases. In K. Jain & J. B. T.-N. for T. and D. of I. D. Ahmad (Eds.), *Developments*

- in *Microbiology* (pp. 127–149). Academic Press. <https://doi.org/https://doi.org/10.1016/B978-0-323-91201-3.00007-4>
- Jiang, L., Lee, H. W., and Loo, S. C. J. (2020). Therapeutic lipid-coated hybrid nanoparticles against bacterial infections. *RSC Advances*, **10**(14), 8497–8517. <https://doi.org/10.1039/c9ra10921h>
- Johnston, S. C., Ricks, K. M., Lakkhal-Naouar, I., Jay, A., Subra, C., Raymond, J. L., King, H. A. D., Rossi, F., Clements, T. L., Fetterer, D., Tostenson, S., Cincotta, C. M., Hack, H. R., Kuklis, C., Soman, S., King, J., Peachman, K. K., Kim, D., Chen, W.-H., ... Pitt, M. L. M. (2022). A SARS-CoV-2 Spike Ferritin Nanoparticle Vaccine Is Protective and Promotes a Strong Immunological Response in the Cynomolgus Macaque Coronavirus Disease 2019 (COVID-19) Model. *Vaccines*, **10**(5), 717. <https://doi.org/10.3390/vaccines10050717>
- Joshi, A. S., Singh, P., and Mijakovic, I. (2020). Interactions of Gold and Silver Nanoparticles with Bacterial Biofilms: Molecular Interactions behind Inhibition and Resistance. *International Journal of Molecular Sciences*, **21**(20), 7658. <https://doi.org/10.3390/ijms21207658>
- Joyce, M. G., King, H. A. D., Naouar, I. E., Ahmed, A., Peachman, K. K., Cincotta, C. M., Subra, C., Chen, R. E., Thomas, P. V., Chen, W.-H., Sankhala, R. S., Hajduczki, A., Martinez, E. J., Peterson, C. E., Chang, W. C., Choe, M., Smith, C., Lee, P. J., Headley, J. A., ... Modjarrad, K. (2021). Efficacy of a Broadly Neutralizing SARS-CoV-2 Ferritin Nanoparticle Vaccine in Nonhuman Primates. In *bioRxiv: the preprint server for biology*. <https://doi.org/10.1101/2021.03.24.436523>
- Kalantari, K., Mostafavi, E., Afifi, A. M., Izadiyan, Z., Jahangirian, H., Raffie-Moghaddam, R., and Webster, T. J. (2020). Wound dressings functionalized with silver nanoparticles: promises and pitfalls. *Nanoscale*, **12**(4), 2268–2291. <https://doi.org/10.1039/C9NR08234D>
- Kaminskas, L. M., McLeod, V. M., Kelly, B. D., Sberna, G., Boyd, B. J., Williamson, M., Owen, D. J., and Porter, C. J. H. (2012). A comparison of changes to doxorubicin pharmacokinetics, antitumor activity, and toxicity mediated by PEGylated dendrimer and PEGylated liposome drug delivery systems. *Nanomedicine: Nanotechnology, Biology and Medicine*, **8**(1), 103–111. <https://doi.org/https://doi.org/10.1016/j.nano.2011.05.013>
- Kaur, I. P., Kakkar, V., Deol, P. K., Yadav, M., Singh, M., and Sharma, I. (2014). Issues and concerns in nanotech product development and its commercialization. *Journal of Controlled Release*, **193**, 51–62. <https://doi.org/https://doi.org/10.1016/j.jconrel.2014.06.005>
- Kciuk, M., Marciniak, B., and Kontek, R. (2020). Irinotecan-Still an Important Player in Cancer Chemotherapy: A Comprehensive Overview. *International Journal of Molecular Sciences*, **21**(14), 4919. <https://doi.org/10.3390/ijms21144919>
- Khalaj-Hedayati, A., Chua, C. L. L., Smooker, P., and Lee, K. W. (2020). Nanoparticles in influenza subunit vaccine development: Immunogenicity enhancement. *Influenza and Other Respiratory Viruses*, **14**(1), 92–101. <https://doi.org/https://doi.org/10.1111/irv.12697>
- Khanna, P., Ong, C., Bay, B. H., and Baeg, G. H. (2015). Nanotoxicity: An Interplay of Oxidative Stress, Inflammation and Cell Death. *Nanomaterials*, **5**(3), 1163–1180. <https://doi.org/10.3390/nano5031163>
- Kim, E.-M., and Jeong, H.-J. (2017). Current Status and Future Direction of Nanomedicine: Focus on Advanced Biological and Medical Applications. *Nuclear Medicine and Molecular Imaging*, **51**(2), 106–117. <https://doi.org/10.1007/s13139-016-0435-8>
- Kis, Z. (2022). Stability Modelling of mRNA Vaccine Quality Based on Temperature Monitoring throughout the Distribution Chain. *Pharmaceutics*, **14**(2), 430. <https://doi.org/10.3390/pharmaceutics14020430>
- Kotcherlakota, R., Vydiyam, K., Jeyalakshmi Srinivasan, D., Mukherjee, S., Roy, A., Kuncha, M., Rao, T. N., Sistla, R., Gopal, V., and Patra, C. R. (2019). Restoration of p53 Function in Ovarian Cancer Mediated by Gold Nanoparticle-Based EGFR Targeted Gene Delivery System. *ACS Biomaterials Science & Engineering*, **5**(7), 3631–3644. <https://doi.org/10.1021/acsbomaterials.9b00006>
- Kowalczyk, M., Banach, M., and Rysz, J. (2011). Ferumoxytol: a new era of iron deficiency anemia treatment for patients with chronic kidney disease. *Journal of Nephrology*, **24**(6), 717–722. <https://doi.org/10.5301/jn.5000025>
- Kripp, M., and Hofheinz, R.-D. (2008). Treatment of lymphomatous and leukemic meningitis with liposomal encapsulated cytarabine. *International Journal of Nanomedicine*, **3**(4), 397–401. <https://doi.org/10.2147/ijn.s3259>
- Kumar, A., and Han, S. S. (2021). Enhanced mechanical, biomineralization, and cellular response of nanocomposite hydrogels by bioactive glass and halloysite nanotubes for bone tissue regeneration. *Materials Science and Engineering: C*, **128**, 112236. <https://doi.org/https://doi.org/10.1016/j.msec.2021.112236>
- Kumari, L., Choudhari, Y., Patel, P., Gupta, G. Das, Singh, D., Rosenholm, J. M., Bansal, K. K., and Kurmi, B. Das. (2023). Advancement in Solubilization Approaches: A Step towards Bioavailability Enhancement of Poorly Soluble Drugs. *Life*, **13**(5), 1099. <https://doi.org/10.3390/life13051099>
- Kunkel, A. A., and McHugh, K. J. (2024). Injectable controlled-release systems for the prevention and treatment of infectious diseases. *Journal of Biomedical Materials Research Part A*, **112**(8), 1224–1240. <https://doi.org/https://doi.org/10.1002/jbm.a.37615>
- Lamb, Y. N., and Scott, L. J. (2017). Liposomal Irinotecan: A Review in Metastatic Pancreatic Adenocarcinoma. *Drugs*, **77**(7), 785–792. <https://doi.org/10.1007/s40265-017-0741-1>
- Lancet, J. E., Cortes, J. E., Hogge, D. E., Tallman, M. S., Kovacsovics, T. J., Damon, L. E., Komrokji, R., Solomon, S. R., Kollitz, J. E., Cooper, M., Yeager, A. M., Louie, A. C., and Feldman, E. J. (2014). Phase 2 trial of CPX-351, a fixed 5:1 molar ratio of cytarabine/daunorubicin, vs cytarabine/daunorubicin in older adults with untreated AML. *Blood*, **123**(21), 3239–3246. <https://doi.org/10.1182/blood-2013-12-540971>
- Lee, J., Arun Kumar, S., Jhan, Y. Y., and Bishop, C. J. (2018). Engineering DNA vaccines against infectious diseases. *Acta Biomaterialia*, **80**, 31–47. <https://doi.org/10.1016/j.actbio.2018.08.033>
- Lee, J., Choi, M.-K., and Song, I.-S. (2023). Recent Advances in Doxorubicin Formulation to Enhance Pharmacokinetics and Tumor Targeting. *Pharmaceutics*, **16**(6), 802. <https://doi.org/10.3390/ph16060802>
- Lekshmi, G., Sana, S. S., Nguyen, V.-H., Nguyen, T. H. C., Nguyen, C. C., Le, Q. Van, and Peng, W. (2020). Recent progress in carbon nanotube polymer composites in tissue engineering and regeneration. *International Journal of Molecular Sciences*, **21**(17), 6440. <https://doi.org/10.3390/ijms21176440>
- Li, C., Lee, A., Grigoryan, L., Arunachalam, P. S., Scott, M. K. D., Trisal, M., Wimmers, F., Sanyal, M., Weidenbacher, P. A., Feng, Y., Adamska, J. Z., Valore, E., Wang, Y., Verma, R., Reis, N., Dunham, D., O'Hara, R., Park, H., Luo, W., ... Pulendran, B. (2022). Mechanisms of innate and adaptive immunity to the Pfizer-BioNTech BNT162b2 vaccine. *Nature Immunology*, **23**(4), 543–555. <https://doi.org/10.1038/s41590-022-01163-9>
- Li, M., Liang, Z., Chen, C., Yu, G., Yao, Z., Guo, Y., Zhang, L., Bao, H., Fu, D., Yang, X., Wang, H., Xue, C., and Sun, B. (2022). Virus-Like Particle-Templated Silica-Adjuvanted Nanovaccines with Enhanced Humoral and Cellular Immunity. *ACS Nano*, **16**(7), 10482–10495. <https://doi.org/10.1021/acsnano.2c01283>

- Li, X., Peng, X., Zoulikha, M., Boafu, G. F., Magar, K. T., Ju, Y., and He, W. (2024). Multifunctional nanoparticle-mediated combining therapy for human diseases. *Signal Transduction and Targeted Therapy*, **9**(1), 1. <https://doi.org/10.1038/s41392-023-01668-1>
- Liu, G., Lovell, J. F., Zhang, L., and Zhang, Y. (2020). Stimulus-Responsive Nanomedicines for Disease Diagnosis and Treatment. *International Journal of Molecular Sciences*, **21**(17), 6380. <https://doi.org/10.3390/ijms21176380>
- Liu, P., Chen, G., and Zhang, J. (2022). A Review of Liposomes as a Drug Delivery System: Current Status of Approved Products, Regulatory Environments, and Future Perspectives. *Molecules*, **27**(4), 1372. <https://doi.org/10.3390/molecules27041372>
- Liu, Y., Liang, Y., Yuhong, J., Xin, P., Han, J. L., Du, Y., Yu, X., Zhu, R., Zhang, M., Chen, W., and Ma, Y. (2024). Advances in Nanotechnology for Enhancing the Solubility and Bioavailability of Poorly Soluble Drugs. *Drug Design, Development and Therapy*, **18**, 1469–1495. <https://doi.org/10.2147/DDDT.S447496>
- Locke, E., Flores-Garcia, Y., Mayer, B. T., MacGill, R. S., Borate, B., Salgado-Jimenez, B., Gerber, M. W., Mathis-Torres, S., Shapiro, S., King, C. R., and Zavala, F. (2024). Establishing RTS,S/AS01 as a benchmark for comparison to next-generation malaria vaccines in a mouse model. *Npj Vaccines*, **9**(1), 29. <https://doi.org/10.1038/s41541-024-00819-x>
- Lowe, T. L., Agrahari, V., Kannan, R. M., and Kannan, S. (2019). Nanotechnology enabled regenerative medicine for neurological disorders. *Advanced Drug Delivery Reviews*, **148**, 1–2. <https://doi.org/10.1016/j.addr.2019.11.006>
- Lu, S., Zhou, S., Xiang, X., Zhang, B., Xu, Z., Pei, Q., and Xie, Z. (2025). Paclitaxel prodrug nanoparticles boost antitumor efficacy via hitchhiking of human serum albumin. *Journal of Colloid and Interface Science*, **679**, 144–154. <https://doi.org/https://doi.org/10.1016/j.jcis.2024.10.075>
- Lu, W., Yao, J., Zhu, X., and Qi, Y. (2021). Nanomedicines: redefining traditional medicine. *Biomedicine & Pharmacotherapy*, **134**, 111103. <https://doi.org/10.1016/j.biopha.2020.111103>
- Lundstrom, K. (2023). COVID-19 Vaccine Development and Cancer. In *Oncology and COVID 19* (pp. 101–120). CRC Press. <https://doi.org/10.1201/9781003362562>
- Ma, P., and Mumper, R. J. (2013). Paclitaxel Nano-Delivery Systems: A Comprehensive Review. *Journal of Nanomedicine & Nanotechnology*, **4**(2), 1000164. <https://doi.org/10.4172/2157-7439.1000164>
- Madej, M., Kurowska, N., and Strzalka-Mrozik, B. (2022). Polymeric nanoparticles—Tools in a drug delivery system in selected cancer therapies. *Applied Sciences*, **12**(19), 9479. <https://doi.org/10.3390/app12199479>
- Mahanta, A. K., Chaulagain, B., Trivedi, R., and Singh, J. (2024). Mannose-Functionalized Chitosan-Coated PLGA Nanoparticles for Brain-Targeted Codelivery of CBD and BDNF for the Treatment of Alzheimer's Disease. *ACS Chemical Neuroscience*, **5**(21), 4021–4032. <https://doi.org/10.1021/acchemneuro.4c00392>
- Mainini, F., and Eccles, M. R. (2020). Lipid and Polymer-Based Nanoparticle siRNA Delivery Systems for Cancer Therapy. *Molecules*, **25**(11), 2692. <https://doi.org/10.3390/molecules25112692>
- Makwana, V., Karanjia, J., Haselhorst, T., Anoopkumar-Dukie, S., and Rudrawar, S. (2021). Liposomal doxorubicin as targeted delivery platform: Current trends in surface functionalization. *International Journal of Pharmaceutics*, **593**, 120117. <https://doi.org/10.1016/j.ijpharm.2020.120117>
- Malabadi, R. B., Meti, N. T., and Chalannavar, R. K. (2021). Applications of nanotechnology in vaccine development for coronavirus (SARS-CoV-2) disease (Covid-19). *International Journal of Research and Scientific Innovations*, **8**(2), 191–198.
- Manke, A., Wang, L., and Rojanasakul, Y. (2013). Mechanisms of Nanoparticle-Induced Oxidative Stress and Toxicity. *BioMed Research International*, **2013**(1), 942916. <https://doi.org/https://doi.org/10.1155/2013/942916>
- Mateu Ferrando, R., Lay, L., and Polito, L. (2020). Gold nanoparticle-based platforms for vaccine development. *Drug Discovery Today: Technology*, **38**, 57–67. <https://doi.org/https://doi.org/10.1016/j.ddtec.2021.02.001>
- Mehta, M., Bui, T. A., Yang, X., Aksoy, Y., Goldys, E. M., and Deng, W. (2023). Lipid-Based Nanoparticles for Drug/Gene Delivery: An Overview of the Production Techniques and Difficulties Encountered in Their Industrial Development. *ACS Materials Au*, **3**(6), 600–619. <https://doi.org/10.1021/acsmaterialsau.3c00032>
- Miethling-Graff, R., Rumpker, R., Richter, M., Verano-Braga, T., Kjeldsen, F., Brewer, J., Hoyland, J., Rubahn, H.-G., and Erdmann, H. (2014). Exposure to silver nanoparticles induces size- and dose-dependent oxidative stress and cytotoxicity in human colon carcinoma cells. *Toxicology in Vitro*, **28**(7), 1280–1289. <https://doi.org/https://doi.org/10.1016/j.tiv.2014.06.005>
- Milano, G., Innocenti, F., and Minami, H. (2022). Liposomal irinotecan (Onivyde): Exemplifying the benefits of nanotherapeutic drugs. *Cancer Science*, **113**(7), 2224–2231. <https://doi.org/10.1111/cas.15377>
- Mitragotri, S., Anderson, D. G., Chen, X., Chow, E. K., Ho, D., Kabanov, A. V., Karp, J. M., Kataoka, K., Mirkin, C. A., Petrosko, S. H., Shi, J., Stevens, M. M., Sun, S., Teoh, S., Venkatraman, S. S., Xia, Y., Wang, S., Gu, Z., and Xu, C. (2015). Accelerating the Translation of Nanomaterials in Biomedicine. *ACS Nano*, **9**(7), 6644–6654. <https://doi.org/10.1021/acsnano.5b03569>
- Mohamed, N. A., Marei, I., Crovella, S., and Abou-Saleh, H. (2022). Recent Developments in Nanomaterials-Based Drug Delivery and Upgrading Treatment of Cardiovascular Diseases. *International Journal of Molecular Sciences*, **23**(3), 1404. <https://doi.org/10.3390/ijms23031404>
- More, P. R., Pandit, S., Filippis, A. De, Franci, G., Mijakovic, I., and Galdiero, M. (2023). Silver nanoparticles: bactericidal and mechanistic approach against drug resistant pathogens. *Microorganisms*, **11**(2), 369. <https://doi.org/10.3390/microorganisms11020369>
- Mukundan, S., Steigner, M. L., Hsiao, L.-L., Malek, S. K., Tullius, S. G., Chin, M. S., and Siedlecki, A. M. (2016). Ferumoxytol-Enhanced Magnetic Resonance Imaging in Late-Stage CKD. *American Journal of Kidney Diseases : The Official Journal of the National Kidney Foundation*, **67**(6), 984–988. <https://doi.org/10.1053/j.ajkd.2015.12.017>
- Nadeem, A. Y., Shehzad, A., Islam, S. U., Al-Suhaimi, E. A., and Lee, Y. S. (2022). Mosquirix™ RTS, S/AS01 Vaccine Development, Immunogenicity, and Efficacy. *Vaccines*, **10**(5), 713. <https://doi.org/10.3390/vaccines10050713>
- Nakamura, Y., Mochida, A., Choyke, P. L., and Kobayashi, H. (2016). Nanodrug Delivery: Is the Enhanced Permeability and Retention Effect Sufficient for Curing Cancer? *Bioconjugate Chemistry*, **27**(10), 2225–2238. <https://doi.org/10.1021/acs.bioconjchem.6b00437>
- Neely, L. A., Audeh, M., Phung, N. A., Min, M., Suchocki, A., Plourde, D., Blanco, M., Demas, V., Skewis, L. R., Anagnostou, T., Coleman, J. J., Wellman, P., Mylonakis, E., and Lowery, T. J. (2013). T2 Magnetic Resonance Enables Nanoparticle-Mediated Rapid Detection of Candidemia in Whole Blood. *Science Translational Medicine*, **5**(182), 182ra54–182ra54. <https://doi.org/10.1126/scitranslmed.3005377>
- Nguyen, T. T., Mammeri, F., and Ammar, S. (2018). Iron Oxide and Gold Based Magneto-Plasmonic Nanostructures for Medical Applications: A Review. *Nanomaterials*, **8**(3), 149. <https://doi.org/10.3390/nano8030149>
- Nishat, S., Jafry, A. T., Martinez, A. W., and Awan, F. R. (2021). Paper-based microfluidics: Simplified fabrication

- and assay methods. *Sensors and Actuators B: Chemical*, **336**, 129681. <https://doi.org/https://doi.org/10.1016/j.snb.2021.129681>
- Noor, R. (2021). Developmental Status of the Potential Vaccines for the Mitigation of the COVID-19 Pandemic and a Focus on the Effectiveness of the Pfizer-BioNTech and Moderna mRNA Vaccines. *Current Clinical Microbiology Reports*, **8**(3), 178–185. <https://doi.org/10.1007/s40588-021-00162-y>
- Nsairat, H., Khater, D., Sayed, U., Odeh, F., Al Bawab, A., and Alshaer, W. (2022). Liposomes: structure, composition, types, and clinical applications. *Heliyon*, **8**(5), e09394. <https://doi.org/10.1016/j.heliyon.2022.e09394>
- Oliveira, B. B., Ferreira, D., Fernandes, A. R., and Baptista, P. V. (2023). Engineering gold nanoparticles for molecular diagnostics and biosensing. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, **15**(1), e1836. <https://doi.org/10.1002/wnan.1836>
- Operti, M. C., Bernhardt, A., Grimm, S., Engel, A., Figdor, C. G., and Tagit, O. (2021). PLGA-based nanomedicines manufacturing: Technologies overview and challenges in industrial scale-up. *International Journal of Pharmaceutics*, **605**, 120807. <https://doi.org/https://doi.org/10.1016/j.ijpharm.2021.120807>
- Organization, W. H. (n.d.). *Background document on the Novavax (NVX-CoV2373) vaccine against COVID-19: background document to the WHO Interim recommendations for use of the Novavax (NVX-CoV2373) vaccine against COVID-19, 20 December 2021*. World Health Organization. <https://iris.who.int/handle/10665/351165>
- Paggi, R., Cenci, E., De Socio, G. V., Belati, A., Marini, D., Gili, A., Camilloni, B., and Mencacci, A. (2021). Accuracy and Impact on Patient Management of New Tools for Diagnosis of Sepsis: Experience with the T2 Magnetic Resonance Bacteria Panel. *Pathogens*, **10**(9), 1132. <https://doi.org/10.3390/pathogens10091132>
- Pandey, R. K., and Prajapati, V. K. (2018). Molecular and immunological toxic effects of nanoparticles. *International Journal of Biological Macromolecules*, **107**, 1278–1293. <https://doi.org/https://doi.org/10.1016/j.ijbiomac.2017.09.110>
- Pandey, S., Shaikh, F., Gupta, A., Tripathi, P., and Yadav, J. S. (2021). A recent update: solid lipid nanoparticles for effective drug delivery. *Advanced Pharmaceutical Bulletin*, **12**(1), 17–33. <https://doi.org/10.34172/apb.2022.007>
- Paris, J. L., Baeza, A., and Vallet-Regí, M. (2019). Overcoming the stability, toxicity, and biodegradation challenges of tumor stimuli-responsive inorganic nanoparticles for delivery of cancer therapeutics. *Expert Opinion on Drug Delivery*, **16**(10), 1095–1112. <https://doi.org/10.1080/17425247.2019.1662786>
- Parveen, S., Misra, R., and Sahoo, S. K. (2012). Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. *Nanomedicine: Nanotechnology, Biology and Medicine*, **8**(2), 147–166. <https://doi.org/https://doi.org/10.1016/j.nano.2011.05.016>
- Pasinszki, T., Krebsz, M., Tung, T. T., and Losic, D. (2017). Carbon Nanomaterial Based Biosensors for Non-Invasive Detection of Cancer and Disease Biomarkers for Clinical Diagnosis. *Sensors*, **17**(8), 1919. <https://doi.org/10.3390/s17081919>
- Patel, D. M., Patel, N. N., and Patel, J. K. (2021). *Nanomedicine Scale-Up Technologies: Feasibilities and Challenges BT - Emerging Technologies for Nanoparticle Manufacturing* (J. K. Patel & Y. V Pathak (eds.); pp. 511–539). Springer International Publishing. https://doi.org/10.1007/978-3-030-50703-9_24
- Patel, J. K., Patel, A., and Bhatia, D. (2021). Introduction to nanomaterials and nanotechnology. In *Emerging technologies for nanoparticle manufacturing* (pp. 3–23). Springer. https://doi.org/10.1007/978-3-030-50703-9_1
- Pattnaik, A., Sahoo, B. R., Struble, L. R., Borgstahl, G. E. O., Zhou, Y., Franco, R., Barletta, R. G., Osorio, F. A., Petro, T. M., and Pattnaik, A. K. (2023). A Ferritin Nanoparticle-Based Zika Virus Vaccine Candidate Induces Robust Humoral and Cellular Immune Responses and Protects Mice from Lethal Virus Challenge. *Vaccines*, **11**(4), 821. <https://doi.org/10.3390/vaccines11040821>
- Pelaz, B., Alexiou, C., Alvarez-Puebla, R. A., Alves, F., Andrews, A. M., Ashraf, S., Balogh, L. P., Ballerini, L., Bestetti, A., Brendel, C., Bosi, S., Carril, M., Chan, W. C. W., Chen, C., Chen, X., Chen, X., Cheng, Z., Cui, D., Du, J., ... Parak, W. J. (2017). Diverse Applications of Nanomedicine. *ACS Nano*, **11**(3), 2313–2381. <https://doi.org/10.1021/acsnano.6b06040>
- Peri, A. M., Stewart, A., Hume, A., Irwin, A., and Harris, P. N. A. (2021). New Microbiological Techniques for the Diagnosis of Bacterial Infections and Sepsis in ICU Including Point of Care. *Current Infectious Disease Reports*, **23**(8), 12. <https://doi.org/10.1007/s11908-021-00755-0>
- Pinal, R. (2024). Enhancing the Bioavailability of Poorly Soluble Drugs. *Pharmaceutics*, **16**(6), 758. <https://doi.org/10.3390/pharmaceutics16060758>
- Polykretis, P. (2022). Role of the antigen presentation process in the immunization mechanism of the genetic vaccines against COVID-19 and the need for biodistribution evaluations. *Scandinavian Journal of Immunology*, **96**(2), e13160. <https://doi.org/10.1111/sji.13160>
- Prajapati, S. K., and Jain, A. (2020). Dendrimers for advanced drug delivery. In *Advanced Biopolymeric Systems for Drug Delivery*. Springer. https://doi.org/10.1007/978-3-030-46923-8_13
- Predtechenskiy, M. R., Khasin, A. A., Bezrodny, A. E., Bobrenok, O. F., Dubov, D. Y., Muradyan, V. E., Saik, V. O., and Smirnov, S. N. (2022). New perspectives in SWCNT applications: Tuball SWCNTs. Part 1. Tuball by itself—All you need to know about it. *Carbon Trends*, **8**, 100175. <https://doi.org/10.1016/j.cartre.2022.100175>
- Proniewicz, E. (2024). Gold and Silver Nanoparticles as Biosensors: Characterization of Surface and Changes in the Adsorption of Leucine Dipeptide under the Influence of Substituent Changes. *International Journal of Molecular Sciences*, **25**(7), 3720. <https://doi.org/10.3390/ijms25073720>
- Raghav, P. K., Mann, Z., Ahlawat, S., and Mohanty, S. (2022). Mesenchymal stem cell-based nanoparticles and scaffolds in regenerative medicine. *European Journal of Pharmacology*, **918**, 174657. <https://doi.org/https://doi.org/10.1016/j.ejphar.2021.174657>
- Rahman, M. M., Islam, M. R., Akash, S., Harun-Or-Rashid, M., Ray, T. K., Rahaman, M. S., Islam, M., Anika, F., Hosain, M. K., Aovi, F. I., Hemeg, H. A., Rauf, A., and Wilairatana, P. (2022). Recent advancements of nanoparticles application in cancer and neurodegenerative disorders: At a glance. *Biomedicine & Pharmacotherapy*, **153**, 113305. <https://doi.org/https://doi.org/10.1016/j.biopha.2022.113305>
- Raj, T. A. S., Smith, A. M., and Moore, A. S. (2013). Vincristine sulfate liposomal injection for acute lymphoblastic leukemia. *International Journal of Nanomedicine*, **8**, 4361–4369. <https://doi.org/10.2147/IJN.S54657>
- Ray, S., Li, Z., Hsu, C.-H., Hwang, L.-P., Lin, Y.-C., Chou, P.-T., and Lin, Y.-Y. (2018). Dendrimer- and copolymer-based nanoparticles for magnetic resonance cancer theranostics. *Theranostics*, **8**(22), 6322–6349. <https://doi.org/10.7150/thno.27828>
- Riaz, M. K., Riaz, M. A., Zhang, X., Lin, C., Wong, K. H., Chen, X., Zhang, G., Lu, A., and Yang, Z. (2018). Surface Functionalization and Targeting Strategies of

- Liposomes in Solid Tumor Therapy: A Review. *International Journal of Molecular Sciences*, **19**(1), 195. <https://doi.org/10.3390/ijms19010195>
- Ribovski, L., Hamelmann, N. M., and Paulusse, J. M. J. (2021). Polymeric Nanoparticles Properties and Brain Delivery. *Pharmaceutics*, **13**(12), 2045. <https://doi.org/10.3390/pharmaceutics13122045>
- Rivas, G. A., Rodríguez, M. C., Rubianes, M. D., Gutierrez, F. A., Eguílaz, M., Dalmasso, P. R., Primo, E. N., Tettamanti, C., Ramírez, M. L., Montemerlo, A., Gally, P., and Parrado, C. (2017). Carbon nanotubes-based electrochemical (bio)sensors for biomarkers. *Applied Materials Today*, **9**, 566–588. <https://doi.org/https://doi.org/10.1016/j.apmt.2017.10.005>
- Rojekar, S., Pai, R., Abadi, L. F., Mahajan, K., Prajapati, M. K., Kulkarni, S., and Vavia, P. (2021). Dual loaded nanostructured lipid carrier of nano-selenium and Etravirine as a potential anti-HIV therapy. *International Journal of Pharmaceutics*, **607**, 120986. <https://doi.org/10.1016/j.ijpharm.2021.120986>
- Roy, V., LaPlant, B. R., Gross, G. G., Bane, C. L., and Palmieri, F. M. (2009). Phase II trial of weekly nab (nanoparticle albumin-bound)-paclitaxel (nab-paclitaxel) (Abraxane) in combination with gemcitabine in patients with metastatic breast cancer (N0531). *Annals of Oncology: Official Journal of the European Society for Medical Oncology*, **20**(3), 449–453. <https://doi.org/10.1093/annonc/mdn661>
- Rubio-Monterde, A., Quesada-González, D., and Merkoçi, A. (2023). Toward Integrated Molecular Lateral Flow Diagnostic Tests Using Advanced Micro- and Nanotechnology. *Analytical Chemistry*, **95**(1), 468–489. <https://doi.org/10.1021/acs.analchem.2c04529>
- Rusling, J. F., Sotzing, G., and Papadimitrakopoulou, F. (2009). Designing nanomaterial-enhanced electrochemical immunosensors for cancer biomarker proteins. *Bioelectrochemistry (Amsterdam, Netherlands)*, **76**(1–2), 189–194. <https://doi.org/10.1016/j.bioelechem.2009.03.011>
- Salahpour Anarjan, F. (2019). Active targeting drug delivery nanocarriers: Ligands. *Nano-Structures & Nano-Objects*, **19**, 100370. <https://doi.org/https://doi.org/10.1016/j.nanoso.2019.10.0370>
- Salciccia, S., Frisenda, M., Bevilacqua, G., Gobbi, L., Bucca, B., Moriconi, M., Viscuso, P., Gentilucci, A., Mariotti, G., Cattarino, S., Forte, F., Fais, S., Logozzi, M., Sciarra, B., and Sciarra, A. (2023). Exosome Analysis in Prostate Cancer: How They Can Improve Biomarkers' Performance. *Current Issues in Molecular Biology*, **45**(7), 6085–6096. <https://doi.org/10.3390/cimb45070384>
- Sarkar, C., Kommineni, N., Butreddy, A., Kumar, R., Bunekar, N., and Gugulothu, K. (2022). PLGA nanoparticles in drug delivery. In *Nanoengineering of Biomaterials*. Wiley Online Library. <https://doi.org/10.1002/9783527832095.ch8>
- Sathish Sundar, D., Gover Antoniraj, M., Senthil Kumar, C., S. Mohapatra, S., N. Houreld, N., and Ruckmani, K. (2016). Recent trends of biocompatible and biodegradable nanoparticles in drug delivery: A review. *Current Medicinal Chemistry*, **23**(32), 3730–3751. <https://doi.org/10.2174/0929867323666160607103854>
- Schoenmaker, L., Witzigmann, D., Kulkarni, J. A., Verbeke, R., Kersten, G., Jiskoot, W., and Crommelin, D. J. A. (2021). mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability. *International Journal of Pharmaceutics*, **601**, 120586. <https://doi.org/https://doi.org/10.1016/j.ijpharm.2021.12.0586>
- Seidu, T. A., Kutoka, P. T., Asante, D. O., Farooq, M. A., Aolga, R. N., and Bo, W. (2022). Functionalization of nanoparticulate drug delivery systems and its influence in cancer therapy. *Pharmaceutics*, **14**(5), 1113. <https://doi.org/10.3390/pharmaceutics14051113>
- Setia, A., Mehata, A. K., Priya, V., Pawde, D. M., Jain, D., Mahto, S. K., and Muthu, M. S. (2023). Current Advances in Nanotheranostics for Molecular Imaging and Therapy of Cardiovascular Disorders. *Molecular Pharmaceutics*, **20**(10), 4922–4941. <https://doi.org/10.1021/acs.molpharmaceut.3c00582>
- Shah, N. N., Merchant, M. S., Cole, D. E., Jayaprakash, N., Bernstein, D., Delbrook, C., Richards, K., Widemann, B. C., and Wayne, A. S. (2016). Vincristine Sulfate Liposomes Injection (VSLI, Marqibo®): Results From a Phase I Study in Children, Adolescents, and Young Adults With Refractory Solid Tumors or Leukemias. *Pediatric Blood & Cancer*, **63**(6), 997–1005. <https://doi.org/https://doi.org/10.1002/pbc.25937>
- Shah, V., and Belozero, I. (2009). Influence of Metal Nanoparticles on the Soil Microbial Community and Germination of Lettuce Seeds. *Water, Air, and Soil Pollution*, **197**(1), 143–148. <https://doi.org/10.1007/s11270-008-9797-6>
- Shanmugam, K. (2024). Modification of Biodegradable Polymer Nanofibers for Cartilage Tissue Engineering Applications: A Review. *Bone and Arthroscopy Science*, **2**(1), 9–29. <https://doi.org/10.26689/bas.v2i1.5957>
- Shao, J., Griffin, R. J., Galanzha, E. I., Kim, J.-W., Koonce, N., Webber, J., Mustafa, T., Biris, A. S., Nedosekin, D. A., and Zharov, V. P. (2013). Photothermal nanodrugs: potential of TNF-gold nanospheres for cancer theranostics. *Scientific Reports*, **3**(1), 1293. <https://doi.org/10.1038/srep01293>
- Sharma, A., Verwilt, P., Li, M., Ma, D., Singh, N., Yoo, J., Kim, Y., Yang, Y., Zhu, J.-H., Huang, H., Hu, X.-L., He, X.-P., Zeng, L., James, T. D., Peng, X., Sessler, J. L., and Kim, J. S. (2024). Theranostic Fluorescent Probes. *Chemical Reviews*, **124**(5), 2699–2804. <https://doi.org/10.1021/acs.chemrev.3c00778>
- Shen, S., Koonjoo, N., Boele, T., Lu, J., Waddington, D. E. J., Zhang, M., and Rosen, M. S. (2024). Enhancing organ and vascular contrast in preclinical ultra-low field MRI using superparamagnetic iron oxide nanoparticles. *Communications Biology*, **7**(1), 1197. <https://doi.org/10.7150/ntno.86467>
- Sia, Z. R., Miller, M. S., and Lovell, J. F. (2021). Engineered Nanoparticle Applications for Recombinant Influenza Vaccines. *Molecular Pharmaceutics*, **18**(2), 576–592. <https://doi.org/10.1021/acs.molpharmaceut.0c00383>
- Silverman, J. A., and Deitcher, S. R. (2013). Marqibo® (vincristine sulfate liposome injection) improves the pharmacokinetics and pharmacodynamics of vincristine. *Cancer Chemotherapy and Pharmacology*, **71**(3), 555–564. <https://doi.org/10.1007/s00280-012-2042-4>
- Singh, N., Sen Gupta, R., and Bose, S. (2024). A comprehensive review on singlet oxygen generation in nanomaterials and conjugated polymers for photodynamic therapy in the treatment of cancer. *Nanoscale*, **16**(7), 3243–3268. <https://doi.org/10.1039/D3NR05801H>
- Soldado, A., Barrio, L. C., Díaz-Gonzalez, M., de la Escosura-Muñiz, A., and Costa-Fernandez, J. M. (2022). Advances in quantum dots as diagnostic tools. *Advances in Clinical Chemistry*, **107**, 1–40. <https://doi.org/10.1016/bs.acc.2021.07.001>
- Soundararajan, A., Bao, A., Phillips, W. T., Perez, R. 3rd, and Goins, B. A. (2009). [(186)Re]Liposomal doxorubicin (Doxil): in vitro stability, pharmacokinetics, imaging and biodistribution in a head and neck squamous cell carcinoma xenograft model. *Nuclear Medicine and Biology*, **36**(5), 515–524. <https://doi.org/10.1016/j.nucmedbio.2009.02.004>
- Spoială, A., Ilie, C.-I., Motelica, L., Ficaï, D., Semenescu, A., Oprea, O.-C., and Ficaï, A. (2023). Smart magnetic drug delivery systems for the treatment of cancer. *Nanomaterials*, **13**(5), 876. <https://doi.org/10.3390/pharmaceutics15010236>
- Stoumpos, S., Hennessy, M., Vesey, A. T., Radjenovic, A.,

- Kasthuri, R., Kingsmore, D. B., Mark, P. B., and Roditi, G. (2019). Ferumoxytol magnetic resonance angiography: a dose-finding study in patients with chronic kidney disease. *European Radiology*, **29**(7), 3543–3552. <https://doi.org/10.1007/s00330-019-06137-4>
- Subbiah, R., and Guldberg, R. E. (2019). Materials Science and Design Principles of Growth Factor Delivery Systems in Tissue Engineering and Regenerative Medicine. *Advanced Healthcare Materials*, **8**(1), 1801000. <https://doi.org/https://doi.org/10.1002/adhm.201801000>
- Subhan, M. A., Yalamarty, S. S. K., Filipczak, N., Parveen, F., and Torchilin, V. P. (2021). Recent Advances in Tumor Targeting via EPR Effect for Cancer Treatment. *Journal of Personalized Medicine*, **11**(6), 571. <https://doi.org/10.3390/jpm11060571>
- Sun, B., and Xia, T. (2016). Nanomaterial-based vaccine adjuvants. *Journal of Materials Chemistry B*, **4**(33), 5496–5509. <https://doi.org/10.1039/C6TB01131D>
- Swetha, K., Kotla, N. G., Tunki, L., Jayaraj, A., Bhargava, S. K., Hu, H., Bonam, S. R., and Kurapati, R. (2023). Recent Advances in the Lipid Nanoparticle-Mediated Delivery of mRNA Vaccines. *Vaccines*, **11**(3), 658. <https://doi.org/10.3390/vaccines11030658>
- Tarach, P., and Janaszewska, A. (2021). Recent Advances in Preclinical Research Using PAMAM Dendrimers for Cancer Gene Therapy. *International Journal of Molecular Sciences*, **22**(6), 2912. <https://doi.org/10.3390/ijms22062912>
- Taslem Mouroi, J., Awe, A., Jain, S., and Batra, H. (2022). Nucleic Acid Vaccine Platform for DENGUE and ZIKA Flaviviruses. *Vaccines*, **10**(6), 834. <https://doi.org/10.3390/vaccines10060834>
- Thomas, R. G., Surendran, S. P., and Jeong, Y. Y. (2020). Tumor microenvironment-stimuli responsive nanoparticles for anticancer therapy. *Frontiers in Molecular Biosciences*, **7**, 610533. <https://doi.org/10.3389/fmolb.2020.610533>
- Tran, S., DeGiovanni, P.-J., Piel, B., and Rai, P. (2017). Cancer nanomedicine: a review of recent success in drug delivery. *Clinical and Translational Medicine*, **6**(1), 44. <https://doi.org/10.1186/s40169-017-0175-0>
- Vahab, S. A., K I A., M, S., and Kumar, V. S. (2024). Exploring chitosan nanoparticles for enhanced therapy in neurological disorders: a comprehensive review. *Naunyn-Schmiedeberg's Archives of Pharmacology*, **25**(22), 5294. <https://doi.org/10.1007/s00210-024-03507-8>
- Verbeke, R., Hogan, M. J., Loré, K., and Pardi, N. (2022). Innate immune mechanisms of mRNA vaccines. *Immunity*, **55**(11), 1993–2005. <https://doi.org/10.1016/j.immuni.2022.10.014>
- Vieira, I. R. S., Tessaro, L., and Conte-Junior, C. A. (2024). Chapter 10 - Gold nanoparticles for treatment of infectious diseases (P. B. T.-G. N. for D. D. Kesharwani (ed.); pp. 277–303). Academic Press. <https://doi.org/https://doi.org/10.1016/B978-0-443-19061-2.00004-3>
- Vines, J. B., Yoon, J.-H., Ryu, N.-E., Lim, D.-J., and Park, H. (2019). Gold Nanoparticles for Photothermal Cancer Therapy. *Frontiers in Chemistry*, **7**. <https://www.frontiersin.org/journals/chemistry/articles/10.3389/fchem.2019.00167>
- Wagner, A. M., Knipe, J. M., Orive, G., and Peppas, N. A. (2019). Quantum dots in biomedical applications. *Acta Biomaterialia*, **94**, 44–63. <https://doi.org/10.1016/j.actbio.2019.05.022>
- Wang, A. Z., Langer, R., and Farokhzad, O. C. (2012). Nanoparticle delivery of cancer drugs. *Annual Review of Medicine*, **63**, 185–198. <https://doi.org/10.1146/annurev-med-040210-162544>
- Wang, B., Akiba, U., and Anzai, J.-I. (2017). Recent Progress in Nanomaterial-Based Electrochemical Biosensors for Cancer Biomarkers: A Review. *Molecules*, **22**(7), 106. <https://doi.org/10.3390/molecules22071048>
- Wei, C., Chen, X., Ji, J., Xu, Y., He, X., Zhang, H., Mo, Z., and Wang, F. (2023). Urinary exosomal prostate-specific antigen is a noninvasive biomarker to detect prostate cancer: Not only old wine in new bottles. *International Journal of Cancer*, **152**(8), 1719–1727. <https://doi.org/https://doi.org/10.1002/ijc.34388>
- Welch, E. C., Powell, J. M., Clevinger, T. B., Fairman, A. E., and Shukla, A. (2021). Advances in biosensors and diagnostic technologies using nanostructures and nanomaterials. *Advanced Functional Materials*, **31**(44), 2104126. <https://doi.org/10.1002/adfm.202104126>
- Wells, C. M., Harris, M., Choi, L., Murali, V. P., Guerra, F. D., and Jennings, J. A. (2019). Stimuli-Responsive Drug Release from Smart Polymers. *Journal of Functional Biomaterials*, **10**(3), 34. <https://doi.org/10.3390/jfb10030034>
- Wibowo, D., Jorritsma, S. H. T., Gonzaga, Z. J., Evert, B., Chen, S., and Rehm, B. H. A. (2021). Polymeric nanoparticle vaccines to combat emerging and pandemic threats. *Biomaterials*, **268**, 120597. <https://doi.org/10.1016/j.biomaterials.2020.120597>
- Witika, B. A., Poka, M. S., Demana, P. H., Matafwali, S. K., Melamane, S., Malungelo Khamanga, S. M., and Makoni, P. A. (2022). Lipid-Based Nanocarriers for Neurological Disorders: A Review of the State-of-the-Art and Therapeutic Success to Date. *Pharmaceutics*, **14**(4), 836. <https://doi.org/10.3390/pharmaceutics14040836>
- Woodson, T. S., and Jha, S. (2023). Comparison of nanotechnology research for coronaviruses and influenza from 2000 to 2022. *Journal of Nanoparticle Research*, **25**(9), 182. <https://doi.org/10.1007/s11051-023-05831-1>
- Wu, D., Chen, Q., Chen, X., Han, F., Chen, Z., and Wang, Y. (2023). The blood–brain barrier: Structure, regulation and drug delivery. *Signal Transduction and Targeted Therapy*, **8**(1), 217. <https://doi.org/10.1038/s41392-023-01481-w>
- Wu, Y., Vazquez-Prada, K. X., Liu, Y., Whittaker, A. K., Zhang, R., and Ta, H. T. (2021). Recent Advances in the Development of Theranostic Nanoparticles for Cardiovascular Diseases. *Nanotheranostics*, **5**(4), 499–514. <https://doi.org/10.7150/ntno.62730>
- Xia, W., Tao, Z., Zhu, B., Zhang, W., Liu, C., Chen, S., and Song, M. (2021). Targeted Delivery of Drugs and Genes Using Polymer Nanocarriers for Cancer Therapy. *International Journal of Molecular Sciences*, **22**(17), 9118. <https://doi.org/10.3390/ijms22179118>
- Xuan, L., Ju, Z., Skonieczna, M., Zhou, P., and Huang, R. (2023). Nanoparticles-induced potential toxicity on human health: applications, toxicity mechanisms, and evaluation models. *MedComm*, **4**(4), e327. <https://doi.org/10.1002/mco2.327>
- Yadav, T., Kumar, S., Mishra, G., and Saxena, S. K. (2023). Tracking the COVID-19 vaccines: The global landscape. *Human Vaccines & Immunotherapeutics*, **19**(1), 2191577. <https://doi.org/10.1080/21645515.2023.2191577>
- Yao, Y., Zhou, Y., Liu, L., Xu, Y., Chen, Q., Wang, Y., Wu, S., Deng, Y., Zhang, J., and Shao, A. (2020). Nanoparticle-Based Drug Delivery in Cancer Therapy and Its Role in Overcoming Drug Resistance. *Frontiers in Molecular Biosciences*, **7**, 193. <https://doi.org/10.3389/fmolb.2020.00193>
- Yu, B., Tai, H. C., Xue, W., Lee, L. J., and Lee, R. J. (2010). Receptor-targeted nanocarriers for therapeutic delivery to cancer. *Molecular Membrane Biology*, **27**(7), 286–298. <https://doi.org/10.3109/09687688.2010.521200>
- Yukawa, H., Sato, K., and Baba, Y. (2023). Theranostics applications of quantum dots in regenerative medicine, cancer medicine, and infectious diseases. *Advanced Drug Delivery Reviews*, **200**, 114863. <https://doi.org/10.1016/j.addr.2023.114863>
- Zare, S., Kabiri, M., Amini, Y., Najafi, A., Mohammadpour, F., Ayati, S. H., Nikpoor, A. R., and Tafaghodi, M. (2021). Immunological Assessment of Chitosan or Trimethyl Chitosan-Coated PLGA Nanospheres Containing Fusion

- Antigen as the Novel Vaccine Candidates Against Tuberculosis. *AAPS PharmSciTech*, **23**(1), 15. <https://doi.org/10.1208/s12249-021-02146-z>
- Zhang, B., Yang, C., Gao, Y., Wang, Y., Bu, C., Hu, S., Liu, L., Demir, H. V., Qu, J., and Yong, K.-T. (2017). Engineering Quantum Dots with Different Emission Wavelengths and Specific Fluorescence Lifetimes for Spectrally and Temporally Multiplexed Imaging of Cells. *Nanotheranostics*, **1**(1), 131–140. <https://doi.org/10.7150/ntno.18989>
- Zhang, C., Yan, L., Wang, X., Zhu, S., Chen, C., Gu, Z., and Zhao, Y. (2020). Progress, challenges, and future of nanomedicine. *Nano Today*, **35**, 101008. <https://doi.org/https://doi.org/10.1016/j.nantod.2020.101008>
- Zhang, R. X., Wong, H. L., Xue, H. Y., Eoh, J. Y., and Wu, X. Y. (2016). Nanomedicine of synergistic drug combinations for cancer therapy - Strategies and perspectives. *Journal of Controlled Release : Official Journal of the Controlled Release Society*, **240**, 489–503. <https://doi.org/10.1016/j.jconrel.2016.06.012>
- Zhang, X., Meng, Y., Gong, B., Wang, T., Lu, Y., Zhang, L., and Xue, J. (2022). Electrospun nanofibers for manipulating soft tissue regeneration. *Journal of Materials Chemistry B*, **10**(37), 7281–7308. <https://doi.org/10.1039/D2TB00609J>
- Zhao, M., Lei, C., Yang, Y., Bu, X., Ma, H., Gong, H., Liu, J., Fang, X., Hu, Z., and Fang, Q. (2015). Abraxane, the Nanoparticle Formulation of Paclitaxel Can Induce Drug Resistance by Up-Regulation of P-gp. *PLoS One*, **10**(7), e0131429. <https://doi.org/10.1371/journal.pone.0131429>
- Zhu, M., Wang, R., and Nie, G. (2014). Applications of nanomaterials as vaccine adjuvants. *Human Vaccines & Immunotherapeutics*, **10**(9), 2761–2774. <https://doi.org/10.4161/hv.29589>