

REVIEW ARTICLE

Recent Advances in Nanomedicine

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Abstract: Nanomedicine has emerged as a transformative field at the intersection of nanotechnology and medical science, operating at the molecular scale to revolutionize healthcare delivery. The integration of engineered nanostructures with biological systems has enabled precise drug delivery mechanisms, enhanced diagnostic capabilities, and innovative therapeutic approaches. Sophisticated nanocarriers and smart materials have demonstrated remarkable success in targeted drug delivery, particularly in cancer treatment, where they effectively overcome biological barriers while minimizing systemic toxicity. Advanced nanoplateforms have facilitated real-time disease monitoring, early detection of biomarkers, and personalized therapeutic interventions. The field has progressed significantly in developing nano-based vaccines, neurological treatments, and cardiovascular applications. Artificial intelligence and machine learning integration have accelerated the development of tailored therapeutic strategies. However, significant challenges persist in scalability, manufacturing standardization, and regulatory compliance. Safety considerations, including long-term toxicological effects and environmental impact, remain critical areas requiring thorough investigation. Recent innovations in nano-bioengineering and molecular imaging have opened new avenues for treating previously intractable diseases. The convergence of multiple scientific disciplines in nanomedicine continues to drive innovations in drug delivery, diagnostics, and regenerative medicine, promising more effective and personalized healthcare solutions for diverse medical conditions.

Keywords: Nanotechnology; Nanoparticles; Nanotherapeutics; Drug Delivery Systems; Theranostics; Nanodiagnostics; Precision Medicine.

1. Introduction

Nanomedicine represents a paradigm shift in healthcare, operating at a scale where the fundamental properties of materials intersect with biological processes. At the nanoscale (1-100 nanometers), materials exhibit unique physicochemical properties that can be harnessed for therapeutic and diagnostic purposes [1]. The field emerged from the convergence of nanotechnology, molecular biology, and medical science, offering unprecedented opportunities to address longstanding challenges in healthcare delivery [2]. The evolution of nanomedicine has been driven by the critical need for more precise, effective, and personalized therapeutic approaches.

Traditional medical treatments often face limitations such as poor drug solubility, inadequate tissue distribution, and significant side effects. Nanomedicine addresses these challenges through innovative approaches to drug delivery, disease diagnosis, and therapeutic intervention [3]. The application of nanotechnology in medicine has revolutionized several key areas: targeted drug delivery systems that minimize side effects while maximizing therapeutic efficacy; advanced diagnostic tools capable of detecting diseases at molecular levels; and regenerative medicine approaches that promote tissue repair and regeneration [4]. These advances have been particularly impactful in oncology, where nanoparticle-based treatments have demonstrated superior tumor targeting and reduced systemic toxicity compared to conventional chemotherapy [5].

Recent developments in materials science and bioengineering have expanded the toolkit of nanomedicine, introducing smart materials that respond to specific biological triggers, multifunctional nanoplateforms that combine therapeutic and diagnostic capabilities, and engineered nanostructures that can navigate biological barriers [6]. The integration of artificial intelligence and nanotechnology has further accelerated the development of predictive models for nanoparticle behavior in biological systems [7].

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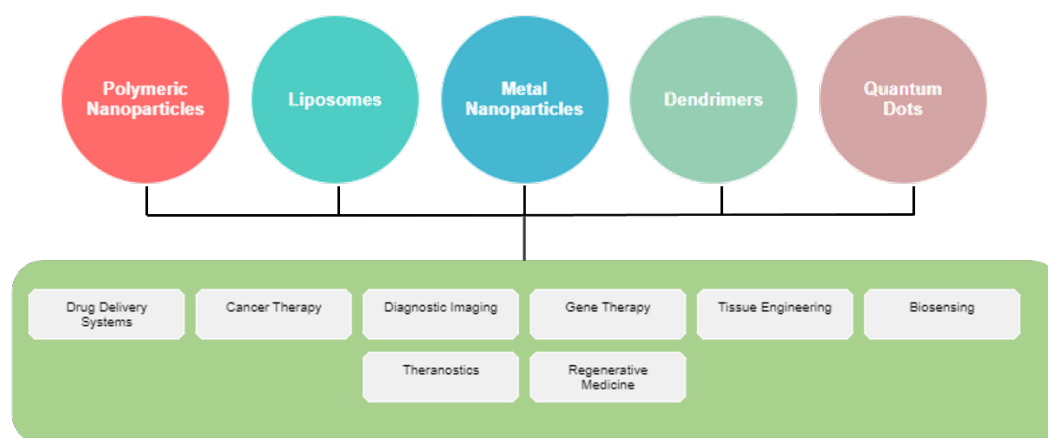


Figure 1. Schematic representation of various nanomedicine platforms and their applications in healthcare

Despite significant progress, the field faces important challenges related to scalability, reproducibility, and regulatory compliance. Understanding the long-term effects of nanomaterials on human health and the environment remains crucial for their safe implementation in clinical settings [8]. Additionally, the complex nature of biological systems necessitates continued research into nanoparticle-tissue interactions and their impact on therapeutic outcomes [9-10].



Figure 2. Timeline of major developments in nanomedicine (1990-2024)

2. Nanomedicine

2.1. Principles

The foundation of nanomedicine rests on the unique properties that materials exhibit at the nanoscale. At dimensions between 1-100 nanometers, materials demonstrate distinct physical, chemical, and biological behaviors that differ significantly from their bulk counterparts [11]. These properties include enhanced surface area-to-volume ratios, quantum effects, and altered electronic configurations, which can be exploited for therapeutic purposes [12]. The quantum confinement effects at this scale lead to unique optical, electrical, and magnetic properties that enable novel diagnostic and therapeutic applications.

2.2. Nanoparticle-Biological Interactions

When nanoparticles enter biological systems, they immediately encounter a complex environment of proteins, ions, and biomolecules. The formation of a protein corona around nanoparticles occurs within seconds of exposure to biological fluids, fundamentally altering their surface properties and biological identity [13]. This protein corona composition is dynamic and depends on the nanoparticle's surface chemistry, size, and the biological environment. The nature of these interactions determines the nanoparticle's fate in the body, including its circulation time, cellular uptake, and eventual clearance [14].

2.3. Transport Mechanisms

2.3.1. Passive Transport

The enhanced permeability and retention (EPR) effect represents a cornerstone mechanism in nanomedicine delivery. This phenomenon occurs due to the architectural abnormalities in tumor vasculature, characterized by large fenestrations between endothelial cells and impaired lymphatic drainage. These features allow nanoparticles to preferentially accumulate in tumor tissues [15]. However, the heterogeneity of tumor vasculature and interstitial pressure can significantly impact the effectiveness of passive targeting.

2.3.2. Active Targeting

Surface modification of nanoparticles with specific targeting moieties enables precise recognition of cellular receptors or disease-specific markers. This approach involves conjugating ligands such as antibodies, peptides, or small molecules to the nanoparticle surface. The specificity of these interactions significantly enhances therapeutic efficacy while minimizing off-target effects [16].

Table 1. Targeting mechanisms of nanomedicine

Targeting Mechanism	Components	Cellular uptake	Advantages	Limitations
Passive Targeting	Enhanced Permeability and Retention (EPR) effect	Accumulation in leaky vasculature; Retention due to poor lymphatic drainage	Non-specific tumor accumulation; Reduced systemic exposure	Variable EPR effect; Limited penetration depth
Active Targeting (Ligand-mediated)	Antibodies; Peptides; Aptamers; Small molecules	Specific cellular recognition; Enhanced cellular uptake; Receptor-mediated endocytosis	Improved selectivity; Higher therapeutic efficacy; Reduced off-target effects	Cost of ligand production; Immunogenicity risks; Complex manufacturing
Stimuli-Responsive	pH-sensitive; Redox-responsive; Enzyme-responsive; Temperature-sensitive	Triggered release in specific conditions; Response to tumor microenvironment	Controlled drug release; Site-specific activation; Reduced systemic toxicity	Complex design; Stability concerns; Batch variability
Cell-Mediated	Immune cells; Stem cells; Engineered cells	Natural targeting abilities; Dynamic response; Biological barrier crossing	Enhanced tissue penetration; Improved therapeutic index; Natural trafficking	Cell viability issues; Complex manufacturing; High production costs

2.4. Cellular Entry and Drug Release

The cellular internalization of nanoparticles occurs through sophisticated endocytic pathways. Clathrin-mediated endocytosis predominates for particles in the size range of 50-200 nm, while caveolin-mediated endocytosis typically handles smaller particles. The endosomal escape mechanisms are crucial for therapeutic efficacy, particularly for nucleic acid delivery [17]. Drug release kinetics can be modulated through various environmental triggers within cellular compartments, including pH gradients, enzymatic activity, and redox potential differences.

2.5. Drug Design Considerations

2.5.1. Physicochemical Optimization

The rational design of nanomedicine platforms requires careful consideration of multiple parameters that influence their biological performance. Particle size optimization is crucial for achieving desired biodistribution patterns and cellular uptake efficiency. Surface charge modifications affect protein corona formation and cellular interactions, while shape engineering can enhance circulation time and tissue penetration [18].

2.5.2. Biological Retention

Circulation time can be extended through surface modification with hydrophilic polymers, while immune system interactions can be modulated through careful surface engineering. Biodegradation pathways must be considered to ensure safe clearance from the body [19].

2.5.3. Smart Design Integration

Modern nanomedicine platforms incorporate intelligent features that respond to specific biological or external stimuli. These systems can achieve precisely controlled drug release profiles, respond to disease-specific markers, and enable real-time monitoring of therapeutic responses. The integration of multiple functionalities within a single platform has led to the development of theranostic systems that combine therapeutic and diagnostic capabilities [20].

Table 2. Design parameters and their therapeutic outcomes

Parameter	Specifications	Impact	Optimization	Outcome
Size	10-200 nm; Monodisperse distribution	Cellular uptake efficiency; Biodistribution pattern; Clearance route	Application-specific sizing; Organ targeting requirements; Filtration thresholds	Circulation time; Tissue penetration; Elimination rate
Surface Chemistry	Charge; Hydrophobicity; Surface modification	Protein corona formation; Immune recognition; Membrane interaction	Stability requirements; Stealth properties; Targeting efficiency	Cellular uptake; Blood compatibility; Target affinity
Material Composition	Polymers; Lipids; Inorganic materials; Hybrid systems	Biodegradability; Biocompatibility; Drug release kinetics	Drug loading capacity; Release mechanisms; Degradation rate	Therapeutic efficacy; Safety profile; Manufacturing feasibility
Morphology	Spherical; Rod-like; Disc-shaped; Complex structures	Cellular internalization; Flow dynamics; Tissue distribution	Shape-dependent effects; Stability considerations; Production complexity	Circulation behavior; Cell interaction; Biodistribution

3. Advantages of Nanomedicine

3.1. Advanced Drug Delivery

Nanomedicine has revolutionized drug delivery through enhanced targeting capabilities and improved therapeutic indices. The precise control over drug release kinetics enables sustained therapeutic concentrations while minimizing peak-related toxicities [21]. Nanocarriers effectively protect therapeutic agents from premature degradation and enhance their stability in biological environments. The ability to overcome biological barriers, including the blood-brain barrier and cellular membranes, has opened new avenues for treating previously intractable conditions [22].

3.2. Enhanced Bioavailability and Pharmacokinetics

Nanoformulations significantly improve the bioavailability of poorly water-soluble drugs through various mechanisms. Surface modification techniques and advanced particle engineering enable enhanced drug solubility and controlled release profiles. The increased surface area-to-volume ratio of nanoparticles promotes better dissolution rates and absorption across biological membranes. These improvements in pharmacokinetic properties allow for reduced dosing frequency and improved patient compliance [23].

3.3. Diagnosis and Real-Time Monitoring

The integration of diagnostic capabilities within nanomedicine platforms has transformed disease detection and monitoring. Nanosensors exhibit unprecedented sensitivity in detecting biomarkers at extremely low concentrations, enabling early disease diagnosis. Advanced imaging capabilities through quantum dots and magnetic nanoparticles provide high-resolution visualization

of disease progression and therapeutic responses. The ability to perform real-time monitoring allows for dynamic adjustment of treatment strategies based on individual patient responses [24].

Table 3. Comparison of conventional diagnostics versus nanodiagnostics

Parameter	Conventional Diagnostics	Nanodiagnostics	Significance
Sensitivity	Limited detection threshold; Variable accuracy; Single analyte detection	Enhanced sensitivity; Multiplexed detection; Lower detection limits	Earlier disease detection; Improved monitoring; Better treatment outcomes
Specificity	Cross-reactivity issues; Background interference; Limited molecular targeting	Molecular-level specificity; Reduced false positives; Multiple target detection	More accurate diagnosis; Reduced misdiagnosis; Targeted therapy selection
Sample Requirements	Large sample volumes; Complex preparation; Multiple testing needs	Minimal sample volume; Simple preparation; Integrated analysis	Less invasive; Rapid results; Cost-effective
Time to Result	Hours to days; Multiple steps; Laboratory dependent	Minutes to hours; Automated processes; Point-of-care capable	Faster treatment decisions; Improved patient care; Reduced hospital stays
Cost	Equipment-dependent; Regular maintenance; Skilled personnel	Initial higher cost; Reduced per-test cost; Minimal maintenance	Long-term cost savings; Improved accessibility; Better resource utilization
Clinical Integration	Established protocols; Limited flexibility; Separate systems	Multimodal capability; Customizable platforms; Integrated systems	Comprehensive diagnosis; Personalized medicine; Improved workflow

3.4. Theranostic Applications

The convergence of therapeutic and diagnostic capabilities in single nanoplateforms represents a significant advancement in personalized medicine. These theranostic systems enable simultaneous treatment and monitoring, providing immediate feedback on therapeutic efficacy. The ability to combine multiple therapeutic modalities, such as chemotherapy and photodynamic therapy, within a single platform enhances treatment outcomes through synergistic effects [25].

3.5. Immunological Benefits

Nanomedicine platforms demonstrate superior capabilities in vaccine development and immunomodulation. Advanced delivery systems protect antigenic material and enhance its presentation to immune cells, resulting in more robust immune responses. The ability to target specific immune cell populations enables precise manipulation of immune responses for both therapeutic and prophylactic applications [26].

3.6. Precision Medicine Implementation

Nanomedicine facilitates the realization of precision medicine through targeted therapeutic approaches. The ability to design nanocarriers that respond to specific molecular signatures enables patient-specific treatment strategies. Integration with genomic and proteomic data allows for the development of personalized therapeutic regimens that account for individual variations in disease progression and treatment response [27].

3.7. Cost-Effectiveness

Despite initial development costs, nanomedicine offers long-term economic benefits through:

3.7.1. Enhanced Therapeutic Efficiency

The improved targeting and reduced dosing requirements lead to more efficient use of therapeutic agents. Reduced side effects and complications result in decreased healthcare management costs. The ability to combine multiple therapeutic modalities in single platforms optimizes resource utilization [28].

3.7.2. Treatment Optimization

Real-time monitoring capabilities enable dynamic adjustment of treatment protocols, reducing wastage and improving outcomes. The potential for outpatient administration of complex therapeutics reduces hospitalization costs. Extended drug stability and controlled release properties minimize the frequency of drug administration [29].

Table 4. Cost to Benefit analysis of nanomedicine implementation

Economic Factor	Initial Phase (1-3 years)	Mid-term Impact (3-5 years)	Long-term Impact (5-10 years)	Cost-Benefit Ratio
Research & Development Costs	High investment in infrastructure; Equipment costs \$10-50M; Personnel training	Reduced development costs; Process optimization; Scale-up efficiency	Standardized protocols; Automated processes; Reduced per-unit costs	1:3 (Long-term ROI)
Manufacturing Costs	Complex production lines; Quality control systems; Raw material expenses	Improved batch consistency; Reduced waste; Optimized production	Economies of scale; Automated manufacturing; Reduced labor costs	1:4 (Production efficiency)
Healthcare System Impact	Implementation costs; Staff training; Infrastructure adaptation	Reduced hospitalization time; Better patient outcomes; Lower treatment costs	Preventive care savings; Reduced chronic disease burden; Improved healthcare efficiency	1:5 (Healthcare savings)
Market Growth	Limited market penetration; High product costs; Regulatory expenses	Expanding market share; Increased competition; Price stabilization	Global market adoption; Diverse product portfolio; Competitive pricing	1:6 (Market returns)
Insurance Coverage	Limited coverage; High co-payments; Restricted access	Increased coverage options; Risk-sharing models; Value-based pricing	Standard coverage; Reasonable co-payments; Broad accessibility	1:3 (Insurance savings)

3.7.3. Environmental Sustainability

Nanomedicine contributes to environmental sustainability through reduced waste generation and improved manufacturing efficiency. The development of biodegradable nanocarriers minimizes environmental impact, while precise targeting reduces the release of therapeutic agents into the environment [30].

4. Limitations of nanomedicine

4.1. Manufacturing and Scale-up

Industrial-scale production of nanomedicines faces significant challenges in maintaining consistent quality and reproducibility. The complex manufacturing processes require precise control over numerous parameters to ensure batch-to-batch uniformity. Variations in particle size distribution, surface properties, and drug loading efficiency can significantly impact therapeutic efficacy. The transition from laboratory-scale production to commercial manufacturing often encounters technical hurdles in maintaining product specifications while achieving cost-effectiveness [31].

4.2. Standardization

The regulatory landscape for nanomedicine approval remains complex due to their unique properties and behavior. Current regulatory frameworks struggle to adequately address the novel characteristics of nanotherapeutics, leading to prolonged approval processes. The lack of standardized protocols for characterization and quality control poses challenges in establishing regulatory guidelines. International harmonization of regulatory requirements adds another layer of complexity to the commercialization process [32].

4.3. Safety

4.3.1. Long-term Effects

The long-term impact of nanoparticles on biological systems remains incompletely understood. Concerns exist regarding potential accumulation in organs and tissues, particularly for non-biodegradable materials. The interaction between nanoparticles and the immune system may lead to unexpected immunological responses or chronic inflammation. The potential for nanoparticles to cross biological barriers, including the blood-brain barrier, raises concerns about unintended neurological effects [33].

4.3.2. Environmental Impact

The environmental fate of nanomaterials poses significant concerns for ecosystem health. The potential accumulation of nanoparticles in environmental matrices and their impact on various organisms requires careful consideration. The challenges in detecting and quantifying nanoparticles in environmental samples complicate risk assessment efforts [34].

Table 5. Environmental and biological risk assessment parameters

Risk Category	Assessment Parameters	Monitoring Methods	Mitigation Strategies	Safety Threshold
Environmental Persistence	Biodegradation rate; Accumulation patterns; Environmental stability	Environmental sampling; Degradation studies; Bioaccumulation tests	Green synthesis methods; Biodegradable materials; Controlled disposal	<0.1% environmental retention
Ecological Impact	Aquatic toxicity; Soil contamination; Food chain effects	Ecosystem monitoring; Species diversity studies; Biomarker analysis	Eco-friendly designs; Containment systems; Recovery protocols	No significant ecosystem change
Human Exposure	Inhalation risks; Dermal contact; Ingestion pathways	Exposure monitoring; Biomarker testing; Health surveillance	Protective equipment; Exposure controls; Safety protocols	Below OSHA/EPA limits
Biological Interactions	Cellular toxicity; Organ accumulation; Immune response	In vitro testing; Animal studies; Clinical monitoring	Design optimization; Safety screening; Risk stratification	No significant adverse effects
Waste Management	Disposal methods; Environmental leaching; Treatment protocols	Waste tracking; Leachate analysis; Treatment efficiency	Specialized disposal; Recycling programs; Decontamination	Zero harmful releases

4.4. Stability

Maintaining the stability of nanomedicine formulations during storage and administration presents significant challenges. Physical instability can lead to particle aggregation or changes in surface properties, affecting therapeutic efficacy. Chemical stability concerns include drug leakage and degradation of surface modifications [35].

4.5. Biological Barriers

Despite advances in design strategies, overcoming certain biological barriers remains challenging. The variability in the enhanced permeability and retention (EPR) effect among different tumor types limits the effectiveness of passive targeting. The presence of biological barriers, such as mucus layers and cellular membranes, can impede efficient drug delivery [36].

4.6. Economic Constraints

4.6.1. Development Costs

The high costs associated with nanomedicine development and characterization pose significant barriers to commercialization. Extensive preclinical testing requirements and complex manufacturing processes contribute to elevated development expenses. The need for specialized equipment and expertise adds to the overall cost burden [37].

4.6.2. Market Access

The high production costs often translate to expensive final products, limiting market access and patient affordability. Insurance coverage and reimbursement policies for nanomedicine-based treatments remain inconsistent across different healthcare systems [38].

4.7. Clinical Challenges

4.7.1. Efficacy

Demonstrating consistent therapeutic efficacy in clinical settings presents unique challenges. The complexity of biological systems and individual patient variations can affect treatment outcomes. The need for long-term clinical studies to establish safety and efficacy profiles delays market entry [39].

4.7.2. Patient-Specific factors

Individual variations in disease progression and patient characteristics can impact treatment effectiveness. The development of personalized nanomedicine approaches requires consideration of genetic and environmental factors. The complexity of patient-specific optimization poses challenges in clinical implementation [40].

5. Emerging trends in nanomedicine

5.1. Advanced Materials and Designs

The evolution of nanomedicine is being driven by breakthroughs in materials science and engineering. DNA-based nanostructures are emerging as programmable platforms for drug delivery and biosensing, offering unprecedented control over molecular interactions. Smart materials incorporating stimuli-responsive elements enable dynamic adaptation to biological conditions. The development of bio-inspired materials that mimic natural cellular processes promises enhanced biocompatibility and therapeutic efficiency [41].

5.2. Artificial Intelligence

5.2.1. Predictive Modeling:

Machine learning algorithms are revolutionizing nanoparticle design and optimization. Advanced computational models enable prediction of nanoparticle-protein interactions and cellular uptake patterns. AI-driven approaches facilitate rapid screening of formulation parameters and therapeutic combinations [42].

5.2.2. Clinical Decision Support:

Integration of AI with nanomedicine platforms enables real-time therapeutic monitoring and adjustment. Predictive analytics help optimize treatment protocols based on individual patient responses. Machine learning algorithms assist in identifying patient populations most likely to benefit from specific nanotherapeutics [43].

Table 6. Applications of AI in development of nanomedicine

AI Application	Technologies Used	Benefits	Challenges	Benefits
Drug Design & Screening	Machine Learning; Deep Neural Networks; Molecular Modeling	Faster candidate identification; Reduced failure rates; Cost optimization	Data quality; Computing power; Algorithm validation	50% reduction in development time
Manufacturing Process Optimization	Reinforcement Learning; Process Control AI; Quality Prediction	Improved yield; Quality consistency; Real-time adjustments	Sensor integration; Process complexity; System reliability	30% improvement in production efficiency
Clinical Decision Support	Natural Language Processing; Predictive Analytics; Pattern Recognition	Personalized treatment; Better outcomes; Reduced errors	Integration with existing systems; Data privacy; User adoption	40% improvement in treatment accuracy
Patient Monitoring	IoT Integration; Real-time Analytics; Predictive Modeling	Early intervention; Remote monitoring; Improved compliance	Device compatibility; Data security; Alert accuracy	60% faster response to adverse events
Quality Control	Computer Vision; Spectral Analysis; Anomaly Detection	Automated inspection; Consistent quality; Reduced waste	Hardware requirements; Validation protocols; Training needs	90% defect detection rate

5.3. Precision Medicine

5.3.1. Molecular Profiling Integration

The convergence of nanomedicine with genomics and proteomics enables highly personalized therapeutic approaches. Nanoplatfroms designed to respond to specific molecular signatures allow for patient-tailored treatments. Advanced diagnostic capabilities facilitate real-time monitoring of disease progression and therapeutic response [44].

5.3.2. Multi-modal Therapeutic Platforms

Development of integrated platforms combining multiple therapeutic modalities within single nanocarriers. Synergistic approaches incorporating conventional therapeutics with emerging treatment modalities. Implementation of adaptive therapeutic systems that respond to disease evolution [45].

5.4. Emerging Applications

5.4.1. Regenerative Medicine:

Nanomaterials are increasingly being utilized in tissue engineering and regenerative medicine applications. Advanced scaffolds incorporating bioactive nanoparticles promote tissue regeneration and wound healing. Controlled release of growth factors and cellular signals enables precise control over tissue development [46].

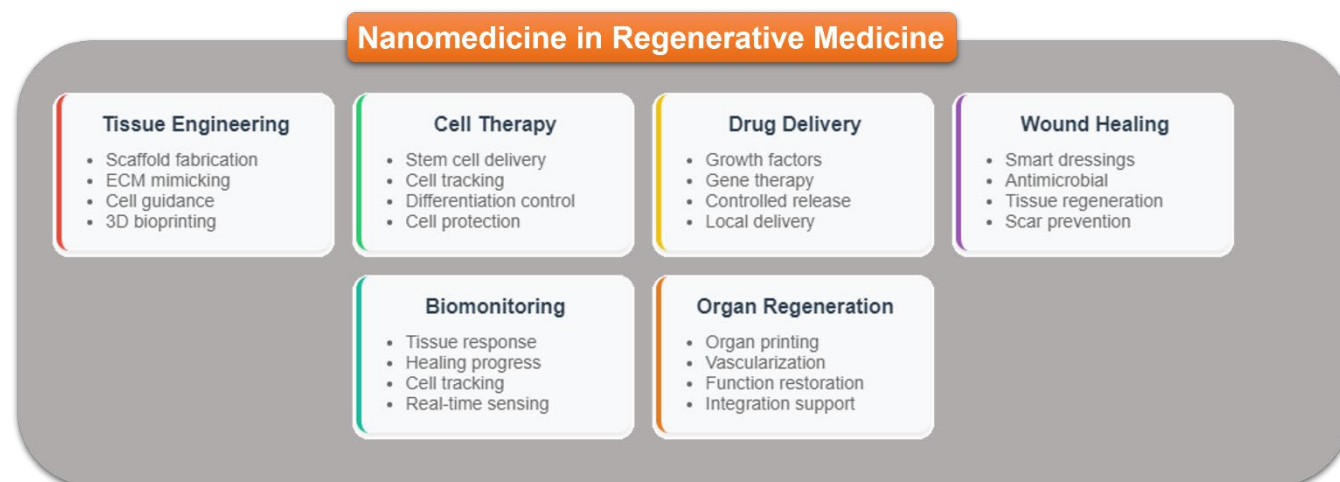


Figure 3. Applications of nanomedicine in regenerative medicine

5.4.2. Neurological Applications

Novel strategies for crossing the blood-brain barrier are expanding treatment options for neurological disorders. Development of targeted nanocarriers for neurodegenerative disease therapy. Integration of neural interfaces with nanomaterials for improved brain-computer interaction [47].

5.5. Manufacturing trends

5.5.1. Continuous Flow Production

Implementation of continuous manufacturing processes for improved scalability and consistency. Advanced quality control systems enabling real-time monitoring of production parameters. Integration of automated systems for enhanced production efficiency [48].

5.5.2. Green Manufacturing:

Development of environmentally sustainable production methods. Implementation of waste reduction strategies and eco-friendly materials. Optimization of energy efficiency in manufacturing processes [49].

6. Conclusion

Nanomedicine represents a transformative approach in healthcare, fundamentally changing our ability to diagnose, treat, and monitor diseases. The field has progressed from theoretical concepts to clinical applications, demonstrating significant advantages over conventional therapeutic approaches. The integration of advanced materials, artificial intelligence, and precision medicine principles has expanded the possibilities for personalized treatment strategies. Despite considerable challenges in manufacturing, regulation, and clinical translation, the continuous evolution of nanomedicine technologies offers promising solutions to current limitations. The development of smart, multifunctional platforms, coupled with improved understanding of nano-bio interactions, is leading to more effective and safer therapeutic options.

References

- [1] Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. *Nat Rev Drug Discov.* 2021;20(2):101-124.
- [2] Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. *Nat Rev Cancer.* 2017;17(1):20-37.

- [3] Anselmo AC, Mitragotri S. Nanoparticles in the clinic: An update. *Bioeng Transl Med*. 2019;4(3):e10143.
- [4] Hua S, de Matos MBC, Metselaar JM, Storm G. Current trends and challenges in the clinical translation of nanoparticulate nanomedicines. *Front Pharmacol*. 2018;9:790.
- [5] Faria M, Björnholm M, Thurecht KJ, Kent SJ, Parton RG, Kavallaris M, et al. Minimum information reporting in bio-nano experimental literature. *Nat Nanotechnol*. 2018;13(9):777-785.
- [6] Chen H, Zhang W, Zhu G, Xie J, Chen X. Rethinking cancer nanotheranostics. *Nat Rev Mater*. 2017;2(7):17024.
- [7] Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, et al. Analysis of nanoparticle delivery to tumours. *Nat Rev Mater*. 2016;1(5):16014.
- [8] Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, et al. Nano based drug delivery systems: recent developments and future prospects. *J Nanobiotechnology*. 2018;16(1):71.
- [9] Tran S, DeGiovanni PJ, Piel B, Rai P. Cancer nanomedicine: a review of recent success in drug delivery. *Clin Transl Med*. 2017;6(1):44.
- [10] Bobo D, Robinson KJ, Islam J, Thurecht KJ, Corrie SR. Nanoparticle-based medicines: a review of FDA-approved materials and clinical trials to date. *Pharm Res*. 2016;33(10):2373-2387.
- [11] Pelaz B, Alexiou C, Alvarez-Puebla RA, Alves F, Andrews AM, Ashraf S, et al. Diverse applications of nanomedicine. *ACS Nano*. 2017;11(3):2313-2381.
- [12] Wolfram J, Ferrari M. Clinical cancer nanomedicine. *Nano Today*. 2019;25:85-98.
- [13] Monopoli MP, Bombelli FB, Dawson KA. Nanoparticle coronas take shape. *Nat Nanotechnol*. 2011;6(1):11-12.
- [14] Ke PC, Lin S, Parak WJ, Davis TP, Caruso F. A decade of the protein corona. *ACS Nano*. 2017;11(12):11773-11776.
- [15] Maeda H, Nakamura H, Fang J. The EPR effect for macromolecular drug delivery to solid tumors: Improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo. *Adv Drug Deliv Rev*. 2013;65(1):71-79.
- [16] Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. *Nat Commun*. 2018;9(1):1410.
- [17] Stewart MP, Langer R, Jensen KF. Intracellular delivery by membrane disruption: Mechanisms, strategies, and concepts. *Chem Rev*. 2018;118(16):7409-7531.
- [18] Nel AE, Mädler L, Velegol D, Xia T, Hoek EMV, Somasundaran P, et al. Understanding biophysicochemical interactions at the nano-bio interface. *Nat Mater*. 2009;8(7):543-557.
- [19] Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. *Nat Biotechnol*. 2015;33(9):941-951.
- [20] Yoo J, Park C, Yi G, Lee D, Koo H. Active targeting strategies using biological ligands for nanoparticle drug delivery systems. *Cancers*. 2019;11(5):640.
- [21] Sun Q, Zhou Z, Qiu N, Shen Y. Rational design of cancer nanomedicine: nanoproperty integration and synchronization. *Adv Mater*. 2017;29(14):1606628.
- [22] Li SD, Huang L. Pharmacokinetics and biodistribution of nanoparticles. *Mol Pharm*. 2008;5(4):496-504.
- [23] Dai Q, Wilhelm S, Ding D, Syed AM, Sindhwani S, Zhang Y, et al. Quantifying the ligand-coated nanoparticle delivery to cancer cells in solid tumors. *ACS Nano*. 2018;12(8):8423-8435.
- [24] Cheng Z, Al Zaki A, Hui JZ, Muzykantov VR, Tsourkas A. Multifunctional nanoparticles: cost versus benefit of adding targeting and imaging capabilities. *Science*. 2012;338(6109):903-910.
- [25] Kelkar SS, Reineke TM. Theranostics: combining imaging and therapy. *Bioconjug Chem*. 2011;22(10):1879-1903.
- [26] Smith DM, Simon JK, Baker Jr JR. Applications of nanotechnology for immunology. *Nat Rev Immunol*. 2013;13(8):592-605.
- [27] Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano Lett*. 2010;10(9):3223-3230.
- [28] Ragelle H, Danhier F, Préat V, Langer R, Anderson DG. Nanoparticle-based drug delivery systems: a commercial and regulatory outlook as the field matures. *Expert Opin Drug Deliv*. 2017;14(7):851-864.
- [29] Ventola CL. Progress in nanomedicine: approved and investigational nanodrugs. *P T*. 2017;42(12):742-755.

- [30] Fadeel B, Garcia-Bennett AE. Better safe than sorry: Understanding the toxicological properties of inorganic nanoparticles manufactured for biomedical applications. *Adv Drug Deliv Rev.* 2010;62(3):362-374.
- [31] Valencia PM, Farokhzad OC, Karnik R, Langer R. Microfluidic technologies for accelerating the clinical translation of nanoparticles. *Nat Nanotechnol.* 2012;7(10):623-629.
- [32] Hafner A, Lovrić J, Lakoš GP, Pepić I. Nanotherapeutics in the EU: an overview on current state and future directions. *Int J Nanomedicine.* 2014;9:1005-1023.
- [33] Feliu N, Docter D, Heine M, Del Pino P, Ashraf S, Kolosnjaj-Tabi J, et al. In vivo degeneration and the fate of inorganic nanoparticles. *Chem Soc Rev.* 2016;45(9):2440-2457.
- [34] Nowack B, Bucheli TD. Occurrence, behavior and effects of nanoparticles in the environment. *Environ Pollut.* 2007;150(1):5-22.
- [35] Yadollahi R, Vasilev K, Simovic S. Nanosuspension technologies for delivery of poorly soluble drugs. *J Nanomater.* 2015;2015:216375.
- [36] Sarella PN, Thammana PK. Potential applications of Folate-conjugated Chitosan Nanoparticles for Targeted delivery of Anticancer drugs. *Research Journal of Pharmaceutical Dosage Forms and Technology.* 2023 Oct 1;15(4):281-8.
- [37] Etheridge ML, Campbell SA, Erdman AG, Haynes CL, Wolf SM, McCullough J. The big picture on nanomedicine: the state of investigational and approved nanomedicine products. *Nanomedicine.* 2013;9(1):1-14.
- [38] Caster JM, Patel AN, Zhang T, Wang A. Investigational nanomedicines in 2016: a review of nanotherapeutics currently undergoing clinical trials. *Wiley Interdiscip Rev Nanomed Nanobiotechnol.* 2017;9(1):e1416.
- [39] Park K. Facing the truth about nanotechnology in drug delivery. *ACS Nano.* 2013;7(9):7442-7447.
- [40] Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol.* 2007;2(12):751-760.
- [41] Douglas SM, Bachelet I, Church GM. A logic-gated nanorobot for targeted transport of molecular payloads. *Science.* 2012;335(6070):831-834.
- [42] Zhong Y, Meng F, Deng C, Zhong Z. Ligand-directed active tumor-targeting polymeric nanoparticles for cancer chemotherapy. *Biomacromolecules.* 2014;15(6):1955-1969.
- [43] Tang J, Baxter S, Menon A, Alaarg A, Sanchez-Gaytan BL, Fay F, et al. Immune cell screening of a nanoparticle library improves atherosclerosis therapy. *Proc Natl Acad Sci USA.* 2016;113(44):E6731-E6740.
- [44] Petros RA, DeSimone JM. Strategies in the design of nanoparticles for therapeutic applications. *Nat Rev Drug Discov.* 2010;9(8):615-627.
- [45] Kamaly N, Yameen B, Wu J, Farokhzad OC. Degradable controlled-release polymers and polymeric nanoparticles: mechanisms of controlling drug release. *Chem Rev.* 2016;116(4):2602-2663.
- [46] Lee K, Silva EA, Mooney DJ. Growth factor delivery-based tissue engineering: general approaches and a review of recent developments. *J R Soc Interface.* 2011;8(55):153-170.
- [47] Saraiva C, Praça C, Ferreira R, Santos T, Ferreira L, Bernardino L. Nanoparticle-mediated brain drug delivery: Overcoming blood-brain barrier to treat neurodegenerative diseases. *J Control Release.* 2016;235:34-47.
- [48] Björnholm M, Yan Y, Caruso F. Engineering and evaluating drug delivery particles in microfluidic devices. *J Control Release.* 2014;190:139-149.
- [49] Ding X, Liu J, Li J, Wang F, Wang Y, Song S, et al. Bioresponsive endosomal pH-activatable nanoplatforms for fluorescence diagnosis and chemotherapy of tumors. *Biomaterials.* 2016;83:1-8.