Nanobiotechnology in Regenerative Medicine and Stem Cell Therapy

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Abstract

Nanobiotechnology has transformed regenerative medicine and stem cell therapy by applying nanotechnology to biological systems to improve tissue repair and organ regeneration alongside targeted therapeutic delivery. The unique physicochemical properties of nanomaterials enable effective scaffold creation while facilitating both cell adherence and proliferation which proves essential for tissue engineering. PLGA and PEG represent examples of biodegradable polymeric scaffolds that offer both structural and biochemical support that emulates natural tissue environments. Nanoparticles such as AuNPs and AgNPs deliver controlled drug delivery and function as bioactive cue modulators with antimicrobial protection to produce superior regenerative results. Nanobiotechnology improves stem cell therapy by creating superior cell viability and targeted differentiation while enabling in vivo tracking through SPIONs advanced imaging agents. Nanomaterials contribute to genetic engineering approaches led by CRISPR/Cas9 to maximize effectiveness in stem cell treatments. Current obstacles still exist because they include regulatory challenges and both cytotoxicity concerns and difficulties with scaling up processes for medical applications. Upcoming studies will concentrate on developing better biomaterial surfaces while designing nanomedicines and improving stem cell interaction performance with nanoparticles to enhance therapeutic results.

Keywords: Nanobiotechnology, Nanoparticle, Tissue engineering, Stem cell therapy

Cite this Article as: Abbas N, Kanwal A, Saeed S, Mukwana S, Zahid T, Rai W and Sarfraz S, 2025. Nanobiotechnology in regenerative medicine and stem cell therapy. In: Nisa ZU, Altaf S, Zahra A and Saeed K (eds), Nanobiotech in Holistic Health: Innovations for Integrated Well-being. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 111-117. https://doi.org/10.47278/book.HH/2025.108

A Publication of Unique Scientific Publishers | Chapter No: 25-017 | Received: 25-Jan-2025 Revised: 08-March-2025 Accepted: 01-May-2025

Introduction

Nanotechnology allows the manipulation of materials on the nanoscale, which ranges from 1 to 100 nm, and gives nanomaterials enhanced mechanical, chemical, and biological properties, making them a choice for the regenerative field (Nurbaeva et al., 2024)). Researchers controlled the assembly and functionalization of these materials to produce biomaterials that mimic the natural structure of tissue, essential in tissue engineering (Asghari et al., 2017). Nanobiotechnology is a central aspect of regenerative medicine; it can aid in the development of scaffolding, support tissues, and promote cell adhesion, differentiation, and proliferation (Babu et al., 2024).

The objective of this chapter is to evaluate how tiny technological tools, particularly nano-sized particles, contribute to the improvement of tissue healing and stem cell treatments. It aims to explore the mechanisms through which these nanoparticles aid in repairing damaged tissues and facilitating targeted drug delivery. Furthermore, the chapter investigates how these nano-tools interact with stem cells to enhance therapeutic outcomes and supports advancements in diagnostic and therapeutic approaches for conditions like skin cancer, especially melanoma. Additionally, in this chapter we will address the existing challenges within this emerging field and propose future directions to translate these scientific advancements into practical clinical applications.

Nano Scaffolds and Nanoparticle

The scaffolds, constructed from biodegradable polymers such as PLGA and PEG, can provide a framework for tissue regeneration by allowing cells to grow and function in a microenvironment that closely mimics natural tissues (Chowdhury et al., 2021). These materials could be designed to adjust following the specific needs of the target tissue, providing both the needed physical structure as well as the biochemical signals in regeneration (Becker et al., 2024). Besides this, nanoparticles have greatly contributed to the drug delivery system for regenerative medicine, serving as a mechanism for controlled release that improves the outcomes of therapy (Veronica, Agrawal, Gopenath, Basalingappa, & Gobianand, 2025). For example, metallic nanoparticles such as gold (AuNPs) and silver (AgNPs) have been proven to exhibit antimicrobial activity and, therefore, are very efficient in preventing infection during tissue regeneration and wound healing (Babu et al., 2024; Chittipolu, 2025).

Additionally, nanoparticles can be engineered to boost the biological functionalities of stem cells, which is the central component of regenerative medicine (Trayford, 2025). Such cells have the extraordinary capability of transforming into different cell types that are essential for tissue regeneration (Herawati, 2025). Nanobiotechnology enhances stem cell therapies by promoting the survival of cells, enhancing the process of differentiation, and promoting the movement of stem cells to the appropriate injury site (Chowdhury et al., 2021). This is achieved by using nanoparticle-based drug delivery systems that offer bioactive cues leading stem cells to the damaged tissue, which induce them to proliferate (Asghari et al., 2017). Furthermore, SPIONs are also on their way to being used in regenerative medicine, where stem cells can be tracked in real time. By attaching these nanoparticles to stem cells, researchers can monitor the behavior, migration, and survival of the cells after transplantation, thereby providing valuable data to optimize therapies (Becker et al., 2024). This in-vivo tracking allows for the precise assessment of stem cell function and ensures that stem cells are performing as expected during tissue repair (Glover et al., 2020; Zhang et al., 2018). As shown in figure 1, there are various applications of nanobiotechnology in regenerative medicine ((Haleem et al., 2023).

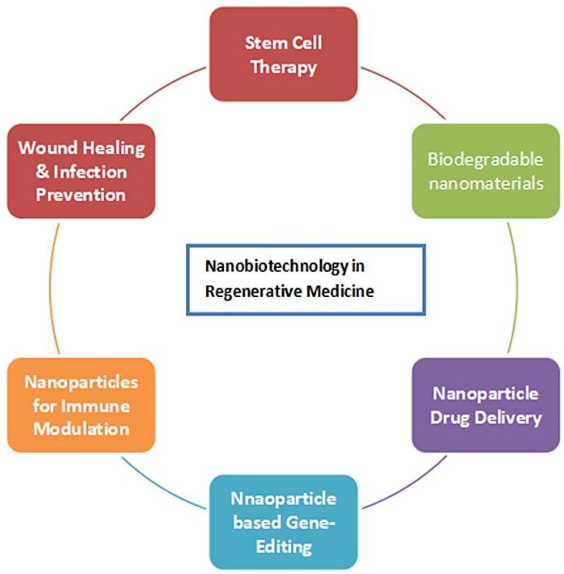

Fig. 1: Overview of nanobiotechnology applications in regenerative medicine, including stem cell therapy, wound healing, immune modulation, biodegradable nanomaterials, nanoparticle drug delivery, and gene editing (Haleem et al., 2023).

Challenges and Future Directions in Nanobiotechnology for Regenerative Medicine

Besides the therapeutic role of nanoparticles, these also decrease risks associated with stem cell therapy like oxidative stress and immune rejection (Aswini et al., 2024). Nanoparticles protect the cells from damaging environmental conditions as they provide a coating that guards the cells against harmful action that might lead to damage to them, hence increasing their efficacy as therapeutic agents. Another very important issue is the regulatory approval of nanobiotechnology-based therapeutics (Bruun et al., 2018). The regulatory agencies, including the FDA, are advancing further with the establishment of clear guidelines on the application of nanoparticles in hospitals. Therefore, it is important that nanobiotechnology therapeutics need to be active and nontoxic to apply to humans (Jain et al., 2025). Growing nanobiotechnology calls for well-defined and standardized testing and approval protocols for these innovative therapeutic approaches (Chaudhury et al., 2014; Glover et al., 2020).

Nanobiotechnology and genetic engineering combined, for instance, gene editing with CRISPR/Cas9, and open new avenues in stem cell therapies. For instance, IONPs can enhance the expression of survival and differentiation genes in stem cells, leading to better outcomes for regenerative therapies (Li et al., 2021). This interplay between nanobiotechnology and genetic engineering will likely be at the forefront of future stem cell therapies and other regenerative treatments (Jain et al., 2025). In the future, nanobiotechnology is bound to play an increasingly important role in regenerative medicine. Improved properties of biomaterials, better stem cell therapies, and effective drug delivery systems will bring a great revolution in tissue regeneration. Although toxicity, regulatory approval, and clinical translation remain to be accomplished, much success with the future of regenerative medicine is still in sight with further advances in personalized nanomedicines and genetic engineering (Asghari et al., 2017; Rajkumar et al., 2024).

Role of Nanoparticles in Stem Cell Therapy

Nanoparticles (NPs) play crucial roles in the regulation of stem cell behavior because of their unique features, including size, shape, surface area, and surface charge. NPs facilitate stem cell therapy through gene delivery. The survival rate of patients suffering from different diseases has improved through surgical procedures and pharmacological treatments but these methods have limited efficacy (Sun et al., 2020). Hence, there is a dire need for regenerative medicine involving stem cells. For therapeutic purposes, stem cell therapy has unprecedented advantages over gene therapy.

Delivery Systems for Therapeutic Agents

Nanoparticle-based delivery systems change the distribution of therapeutic agents such as drugs via target-oriented, site-specific delivery and controlled release of drugs (Table 1) (Yang et al., 2022).

Table 1: Nano delivery systems and their features (Aswini et al., 2024)

Nano delivery systems	Features
Liposomes	Spherical structures, made of the lipid bilayer, carry both hydrophilic and hydrophobic molecules, and target delivery for therapeutic outcomes.
Mesoporous silica nanoparticles (MSNPs)	Silica-based particles, with porous structures, hold an enormous number of therapeutic agents, and prolonged therapeutic effects.
Gold nanoparticles (AuNPs)	Capabilities of surface modification, unmatched precision, and efficacy, and accurate prognosis.
Magnetic nanoparticles (MNPs)	Precise control over stem cell localization, monitoring stem cell responses in real-time, least toxicity, and immune reactions.
Carbon nanotubes (CNTs)	Cylindrical nanostructures offer tailored treatment strategies and enhanced regenerative potential.

Mechanism of Action

Liposomes

Targeted nanoliposomes are used for breast cancer treatment. Their surface is functionalized with targeting agents such as small molecules, peptides, and aptamers which use passive or active targeting in which they can bind either within breast cancer-associated cells or directly to target.

In liposomal drug delivery, cell surface receptors are targeted such as CXCR4 which controls the movement of cells and cancer metastasis after binding to GPCRs (Oshiro et al., 2020). A ligand molecule CXCL12 is a chemoattractant, when a tissue has a high concentration of this molecule, tumor cells with the CXCR4 receptor are drawn to the location. In metastasized breast cancer, encapsulation of pH-responsive liposomes (CXCR4 targeted) is done with Lcn2 siRNA, where Lcn2 protein is silenced to inhibit migration of cells (Nel et al., 2023).

Chitosan Nanoparticles

These are polymeric nanoparticles that have the potential for drug delivery. These nanocarriers are used to treat Parkinson's disease. In a study, Rotigotine, a drug was loaded on chitosan NPs in human neuroblastoma cells SH-SY5Y and delivered through an intranasal route in a rat model (Afzal et al., 2022). These nanostructured lipid carriers allow the drug to go across the blood-brain barrier (BBB). When they reach BBB, stimulus from components on the surface of nanoparticles causes BBB opening resulting in promoting drug conjugates' diffusion into brain tissue. After adsorption on the cell surface, the drug is released from carriers causing an increase in the concentration gradient of the drug thus promoting diffusion of substances into the brain. Capillary endothelial cells of the brain via endocytosis and exocytosis allow penetration of substances into brain tissue (Zorkina et al., 2020). As shown in figure 2, there are multiple steps of how nanoparticles function for therapeutic purposes (Sultana et al., 2022).

Fig. 2: Flowsheet showing the mechanism of action of Nano-based delivery systems for therapeutic agents (Sultana et al., 2022)

Modulation of Stem Cell Behavior through Physical and Chemical Interactions

The mechanical environment of stem cells plays an important role in their differentiation. It includes various factors such as substrate stiffness, topology, extracellular matrix, etc.

Topology and Extracellular Matrix

ECM is comprised of extracellular macromolecules such as elastin, collagen, and fibronectin proteins that are essential for cell survival. When bone marrow mesenchymal stem cells (BMSC) are cultured with various cell types of dECM (cell-derived extracellular matrix), it shows an increased potential (osteogenic and angiogenic) of BMSC (Zhang et al., 2022).

To model ECM, nanoscale materials are widely used and their topology has a great influence on the fate of stem cells (Wu et al., 2021). For peripheral nerve regeneration, nanofibre scaffolds are used which shows that if reduced concentrations of graphene are used in gold nanoparticles in PLC (polycaprolactone) fiber scaffolds, they mimic natural ECM which increases the stimulation of cell differentiation (Jaswal et al., 2020).

Substrate Stiffness

Cells respond to external stimuli through mechanotransduction where physical signals are transduced to chemical ones resulting in cell differentiation to specific lineages (Sun et al., 2022).

Through cytoskeletal contractility, cells sense the hardness of ECM, and its high stiffness leads to BMSCs' differentiation into sweat cells (Wei et al., 2021). Osteogenic differentiation of MSCs is promoted by a harder alginate shell while the softer hydrogel directs differentiation of vascular progenitor cells to endothelial cells.

Shear Stress

The fluid flow in the tissues causes sheer stress to all types of cells. Shear stress can promote the osteogenesis of MSCs. The fate of BMSC differentiation to the osteogenic or chondrogenic cell is also influenced by the rate of fluid sheer stress. Differentiation of BMSCs to myofibroblasts is promoted by shear-stressed groove structures. As illustrated in figure 3, stem cell behaviour is influenced by diverse elements (Wang et al., 2022).

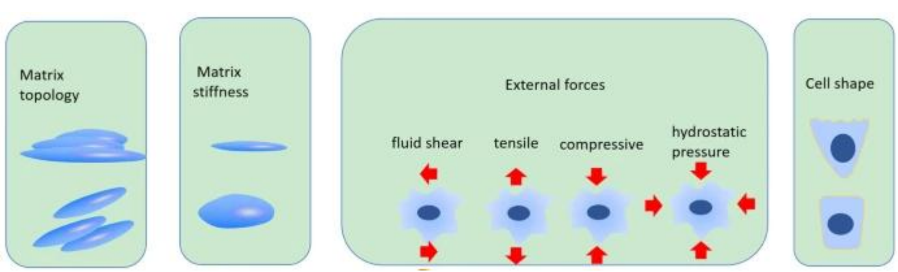

Fig. 3: Various factors that modulate stem cell behavior (Wang et al., 2022)

Types of Nanoparticles

As depicted in figure 4, nanoparticles are classified based on their origin (Khan et al., 2022).

Organic nanoparticles can be made of natural compounds such as proteins, lipids, peptides, or synthetic molecules. Among organic nanoparticles, the most common are polymeric NPs (mostly used in cancer research), liposomes, and dendrimers. Based on origin, they can be natural such as chitosan, or synthetic as synthetic polymer-based nanoparticles (SP-NPs). SP-NPs can be classified into polyesters such as poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly (caprolactone) (PCL) and polyethers such as poly (ethylene glycol) (PEG) (Ruiz et al., 2020).

Natural Nanoparticles

These include lipid-based nanoparticles such as liposomes, and solid lipid nanoparticles. They offer various advantages in terms of loading efficacy, stability, and cellular uptake (Beydar et al., 2024). Polysaccharide-based nanoparticles include chitosan nanoparticles and alginate-based nanoparticles. Natural polyelectrolyte nanoparticles such as chitosan (cationic) and alginate (anionic). Chitosan has mucoadhesive properties as it can electrostatically interact with negatively charged mucosal surfaces and enable better absorption of drugs into the intestine (De Anda et al., 2021).

Synthetic Nanoparticles

These include polymeric nanoparticles composed of synthetic or natural polymers such as PEG, and PLGA. They precisely target specific sites by navigating biological barriers (Beach et al., 2024).

Metallic nanoparticles such as gold nanoparticles, and iron oxide nanoparticles such as superparamagnetic iron oxide nanoparticles (SPIONs). They have large surface area and optical properties, minimal toxicity showing their potential in angiogenic and tumor therapy (Figure 4) (Abdelkawi et al., 2023).

Role of Nanotechnology in Skin Cancer Treatment

Melanoma (skin cancer) is considered a fatal disease worldwide. Skin is formed of two layers; mainly the epidermis and dermis (Hasan et al., 2023; Kumari et al., 2022). The epidermis is the outermost covering that serves as protection. Any change within this specific layer of skin may cause harmful effects leading to the formation of skin cancer (Jain et al., 2022; Urban et al., 2021; Zeng et al., 2023). In the past few years, the mortality rate of melanoma has increased significantly. It has been reported that the occurrence of melanoma is five-fold increased for fifty years in brown people (Saginala et al., 2021). There are two kinds of melanoma non-melanoma skin cancer (NMSC) and melanoma skin cancer (MSC). According to research, MSC is causing a high rate of mortality (American Cancer Society, 2019; Global Cancer Statistics 2018).

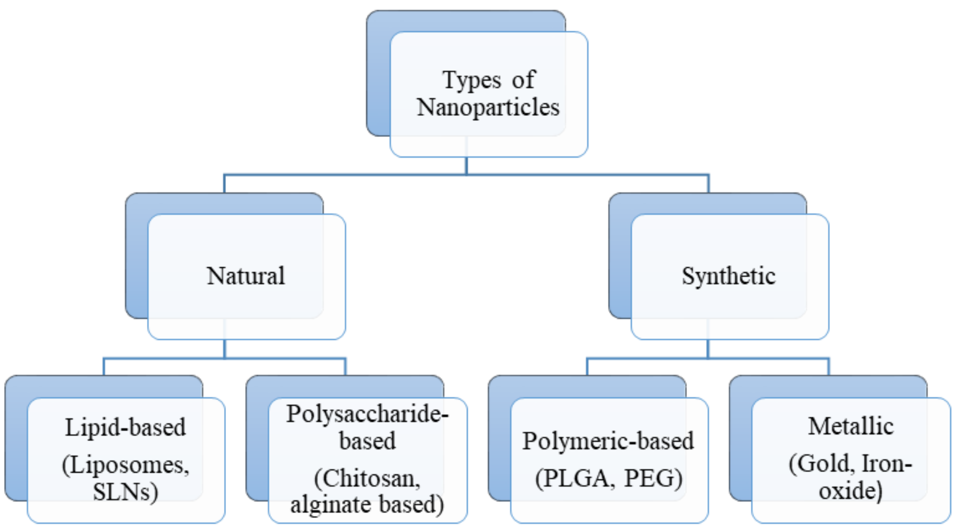

Fig. 4: Types of nanoparticles (Khan et al., 2022)

Melanoma Study in the United States of America (USA)

By the end of 2020, data collected from the global cancer burden (GLOBCAN) revealed an incredible increase in the number of deaths up to 19.3 million, and the mortality rate was found to be 10 million. The type of population and region played a major contributing factor in cancer as per GLOBCAN data (Sung et al., 2020). Non–melanoma was one of the most aggressive types of skin cancer globally found in 1,198,073 patients out of which 722,344 were men and 475,725 were women was 6.2%. Apart from melanoma, other kinds of skin cancers were 63,731 (0.6%). According to a case study carried out in the USA (2024), 150,791 women and 173,844 men were diagnosed with melanoma. It caused a huge number of deaths exceeding 57 thousand organisms (Wild et al., 2020).

Nanotechnology in Diagnosing and Treating Skin Cancer

In recent studies carried out in vitro and in vivo, nanotechnology has been found an appropriate method of treating skin cancer. Nanocarriers and nanomaterials are involved in the development of drug delivery systems causing low side effects because of their large surface and small size characteristics. Antitumor drugs are administered in nanoparticles that pass through cell membranes easily and hit the target cells particularly skin cells showing their maximum effect (Battaglia et al., 2021). The side effects of chemotherapy were reduced owing to the increased activity of anticancer drugs and it played a great role in improving the health of cancer patients. Some other nanoparticles like liposomes, nano micelles, carbon nanotubes, nanoemulsions, and metal nanoparticles are also effective for diagnosing and treatment of skin cancer. These nanoparticles target tumor cells and increase the drug delivery system thus recovering the melanoma (Mir et al., 2022)

Lipid-Based Nanoparticles in Skin Cancer

Drug efficacy has been increased due to lipid formulations that deliver drugs to target cells and organelles thus reducing side effects. Lipid particles are spherical in shape and can dissolve and transport drugs effectively. They include liposomes, ethosomes, niosomes, and solid lipid nanoparticles having distinct characteristics and future implications (Pachauri et al., 2023)

Liposomes

Liposomes are composed of a lipid bilayer having a central space consisting of a transported drug or any other bioactive compound. The use of liposomes has greatly reduced the barriers observed in the administration of chemotherapeutic agents in chemotherapy. Many techniques have been adopted for employing liposomes in curing skin cancer. It includes the use of chemotherapeutic agents, natural polyphenols, and the use of siRNAs in gene therapies to formulate the expression of particular genes of skin cancer (Sing et al., 2023).

In the cell culture of human skin carcinoma A431, chemotherapeutic agents' activity was enhanced by the coating of DOX celecoxib. Liposomes loaded with drugs were efficient in lessening the viability of cancer cells by 99% (Cruz et al., 2022).

Another strategy is found where the surface of liposomes can be modified by binding numerous ligands to it like glycoproteins, immunoglobulin, peptides, transferring, etc thus targeting the receptors in cancer cells. Moreover, liposomes can be used in making vaccines for curing skin cancer (melanoma).

Therapeutic use of Magnetic Nanoparticles (MNPs)

Recently, there has been a lot of interest in the therapeutic use of magnetic nanoparticles (MNPs). Early in the 20th century, Pierre-Ernest Weiss presented the fundamental theory of magnetic particles. Three important components usually make therapeutic MNPs: a coating part that enhances interactions, especially in iron oxide NPs, a magnetite core that serves as a carrier for therapies, and medicines that carry out tasks in vivo. It might have ligands that help to identify particular receptors on the outside of cancer cells. It is important to note that in recent decades, MNPs have been used more frequently to treat cancer (Barani et al, 2023). The advancement of nanotechnology has made it feasible to combine the special qualities and traits of MNPs with those of cancer treatments. MNPs are useful for identifying, diagnosing, and curing malignant tumors. The goal of creating low-toxicity superparamagnetic MNPs for biomedical devices is to reduce complications like embolization or negative cellular or molecular impacts (Bushra et al, 2024).

Conventional hyperthermia has little specificity, because of tissue nonselective heating, and it affects both tumor and healthy cells. By generating local heat and distributing heat around or inside tumor locations, NP-induced hyperthermia can get beyond these barriers. Importantly, a technique known as MNP-based hyperthermia employs MNPs to produce heat in the tumor area when exposed to an alternating magnetic field (AMF) with a frequency range of 100 kHz. The AMF facilitates the transformation of magnetic energy to thermal energy by producing electromagnetic radiation which is absorbed by MNPs. The surrounding tissues become heated as a result. This makes it feasible to precisely deliver heat to the targeted site and helps to treat it. The most promising MNP is the magnetite-based iron oxide (Fe_3O_4). Due to its exceptional biocompatibility and low toxicity, superparamagnetic magnetite (Fe_3O_4), a primary iron oxide, is widely used in biomedical applications (Montazersaheb et al, 2023).

Therapeutic use of Inorganic Nanoparticles

The inefficiency and difficulty in controlling stem cell differentiation remain a significant challenge despite the development of many innovative techniques for inducing cell differentiation. Therefore, a new and alternative approach is required to effectively control the direction of stem cell differentiation in vivo and in vitro in stem cell therapy. The therapy of stem cells may benefit from recent developments in nanotechnology that have produced a novel class of inorganic nanoparticles with special chemical and physical characteristics. Inorganic nanoparticle-based strategies against stem cells have focused on creating drug-delivering nanoparticles, using them to manipulate cell behaviors, and using them to directly induce cell differentiation within the past ten years. (Guo et al, 2022)

Numerous types of inorganic nanoparticles, including upconverting nanoparticles (UCNPs), magnetic nanoparticles (MNPs), quantum dots (QDs), gold nanoparticles (AuNPs), mesoporous silica nanoparticles (MSNs), carbon nanotubes (CNBS), and have been employed in stem cell research and applications. Multipurpose inorganic nanoparticle-based systems have been designed to better understand human diseases create therapeutic strategies for their prevention and treatment, and show significant potential in the field of stem cell biomedical applications. Furthermore, using long-term tracking stem cells in vivo has generated a lot of interest in a method to functionalize inorganic nanoparticles as a nanoprobe towards improved penetration by near-infrared light or nuclear magnetic resonance. (Ma et al, 2023)

Future Perspective

Conventional therapeutic methods and advanced nanoparticle technology have been completely studied. It suggests that though melanoma is curable in its initial stage but needs to be treated fully by the use of the latest technology which is nanotechnology. Melanoma holds about 1.7% of cancer diagnoses globally and is the fifth most occurring disease in the US (Parhi et al., 2021).

There is a dire need to address the challenges for the successful use of nanotechnology in diagnosing and treatment of skin cancer.

The International Agency for Research proposed that cases of skin cancer will reach about 30 million in the next twenty years and need to be controlled. Major contributing factors can be a deteriorated environment, population shift, and migration. Nanotechnology can be found productive in skin cancer treatment via liposomes but further study is required to meet the challenges and optimize the delivery of drug systems (Int et al., 2023).

Challenges and Limitations

Despite the immense potential, there are several challenges and limitations to stem cell therapy:

- Immune Rejection: One of the main challenges in stem cell therapy is immune rejection, especially when using allogeneic stem cells. Autologous stem cells, derived from the patient, are less likely to be rejected but are not always available or suitable (Haworth & Sharpe, 2021).
- Tumorigenicity: Pluripotent stem cells are ESCs and iPSCs which may eventually form a tumor in case they are not properly controlled. Hence, substantial attention focuses on research to ensure that the stem cells differentiate into the desired types of cells without becoming tumorigenic (Chowdhury et al., 2021).

Research is continually being conducted to overcome the existing limitations and increase the diseases that can be treated. Key areas of research in the future include:

- Personalized Stem Cell Therapy: Gene editing tools, such as CRISPR, may allow the generation of personalized stem cells based on the genetic profile of each patient, reducing the risk of immune rejection and increasing therapeutic effectiveness (Jain et al., 2025; Li et al., 2021).
- Advances in Scaffold Design: The development of scaffolds to enhance the support of stem cells in growth and integration into defective tissues will, therefore, be a vital component in improving the efficacy of stem cell treatments (Rajkumar et al., 2024).

Conclusion

Nanoscale biomedical tools are helping doctors improve how tissues heal, how stem cells work, and how we treat cancer. These tiny particles can create environments similar to natural tissues and deliver medicines directly where needed, making treatments more accurate and effective. They can also track healing in real time and help edit genes, opening doors to treatments designed for each patient. Of course, challenges remain - these materials must be safe for the body, avoid triggering immune reactions, and pass regulatory reviews. As the field grows, these microscopic technologies will likely become essential for new healing treatments.

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