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Stem cell therapy: Advances and future directions in regenerative medicine: A review

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Abstract

Stem cell treatment, an important part of regenerative medicine that may change the way many illnesses and injuries are treated in the future. This review article gives an in-depth analysis of the many kinds of stem cells, including adult, induced pluripotent, and embryonic stem cells, as well as their background, properties, and potential for differentiation. Successful hematopoietic stem cell transplantation, tissue engineering, medications for neurological illnesses, and management of autoimmune diseases are only a few of the current applications of stem cells in therapy that we explore. The report also discusses cutting-edge techniques in stem cell research, such as 3D bioprinting, the game-changing CRISPR-Cas9 gene-editing approach, and the manipulation of stem cells using tiny chemicals. However, there are several obstacles on the road to stem cell treatment. We explain how ethical concerns, immunological rejection, and tumorigenicity have influenced public opinion. Future developments in stem cell therapy will be discussed, including the role of stem cell banking, tissue engineering, personalized medicine, and artificial intelligence. In conclusion, despite substantial progress, barriers still need to be eliminated before stem cell treatment can realize its promise to fundamentally alter regenerative medicine.

Keywords: Stem Cell Therapy; Regenerative Medicine; Embryonic Stem Cells (ESCs); Induced Pluripotent Stem Cells (iPSCs); CRISPR-Cas9; Neurological Disorders and Autoimmune Diseases

1. Introduction

1.1. Definition of stem cells and regenerative medicine

Stem cells possess a unique characteristic in their ability to undergo differentiation into many distinct cell lineages. Stem cells serve as a reparative process and a substitute for fully developed tissues. Adult progenitor cells and stem cells play a crucial role in facilitating the body's natural healing process by replenishing impaired adult tissues1. Conversely, embryonic stem cells possess the remarkable ability to differentiate into several specialized cell types over the course of development.

Regenerative medicine is a specialized subject within tissue engineering and molecular biology that focuses on the replacement, modification, or regeneration of human cells, tissues, or organs. Its primary objective is to restore or return these biological components to their normal functioning state. The present region exhibits the capacity to facilitate the regeneration of impaired tissues and organs inside the human body via the augmentation of the healing process of once irreparable organs.

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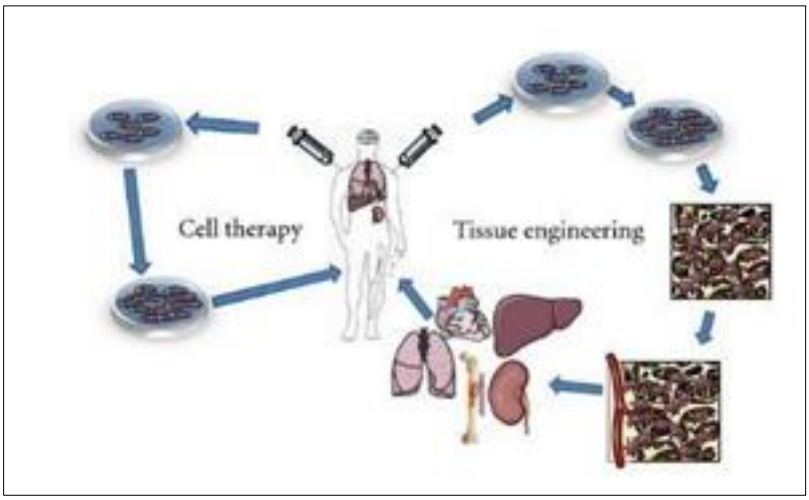

Figure 1 The two approaches to using stem cells in regenerative medicine. In autologous transplantation, stem cells are extracted from the patient; in allogenous transplantation, they are obtained from other donors. The cells are grown in a lab and then either injected into the patient to replace missing cells (a process known as "cell therapy") or deposited into three-dimensional scaffolds (a process known as "tissue engineering") and allowed to develop into the desired cell type. The assembled artificial tissue construct is then inserted into the tissue defect of the patient [28].

1.2. Importance of regenerative medicine in treating various diseases and injuries:

Recent advancements in the field of stem cell research have emerged as a source of optimism for individuals who were previously limited in their access to therapeutic interventions. In the field of regenerative medicine, the significance of human pluripotent stem cells (hPSCs) and multipotent mesenchymal stem cells (MSCs) has seen a notable increase in recent years1. These treatments have the potential to provide assistance in managing a wide range of problems, including but not limited to neurological disorders, respiratory issues, metabolic and endocrine maladies, reproductive abnormalities, skin burns, and cardiovascular troubles.

1.3. Overview of stem cell therapy and its potential applications:

Stem cell therapy refers to the practice of using one's own body's stem cells to heal or prevent illness. Bone marrow transplantation is a subset of hematopoietic stem cell transplantation, the most prevalent kind of stem cell treatment. To rebuild the blood system after cancer therapies and for treating specific immune system and blood system disorders. In addition, studies are being conducted on the potential of stem cell treatments to treat a wide variety of conditions, including neurological illnesses, tissue engineering and organ transplantation and diabetic foot ulcers.

Objectives:

- To offer a thorough examination of the numerous kinds of stem cells, exploring their origins, characteristics, and capacity for differentiation.
- To examine the present uses of stem cells in medicine, emphasizing developments in methods like chemical manipulation, CRISPR-Cas9 gene editing, and 3D bioprinting, while addressing issues including immunological rejection, tumorigenicity, and ethical problems.
- To talk about the potential applications of stem cell therapy in the future, with a focus on the importance of tissue engineering, stem cell banking, personalized medicine and artificial intelligence in regenerative medicine.

2. Materials and Methods

The relevant literature on stem cell therapy and its applications in regenerative medicine was gathered and examined methodically for this review paper. Comprehensive searches of databases, such as PubMed, Scopus, and Google Scholar, were carried out using targeted keywords pertaining to stem cell types, uses, methods, and difficulties. Articles were chosen according to their impact factor, relevancy, and recentness. Other review papers as well as original research pieces were taken into consideration. In order to present a comprehensive picture of the present situation and potential future directions of stem cell therapy in regenerative medicine, the chosen literature was then critically analyzed, synthesized, and arranged into topic sections.

2.1. Types of Stem Cells:

2.1.1. Embryonic stem cells (ESCs)

Characteristics and differentiation potential:

Embryonic stem cells (ESCs), which are pluripotent cells, are obtained from the inner cell mass of the blastocyst. The cells possess the potential for use in tissue engineering and regenerative medicine due to their ability to differentiate into cells of the three germ layers. Recent studies have provided evidence indicating that embryonic stem cells (ESCs) possess the capacity to undergo directed differentiation, leading to the development of many cell lineages, including neurons. According to the findings of Maassen and team [17], it has been shown that stem cells derived from Wharton's Jelly, a gelatinous substance present in the umbilical cord, had the capability to differentiate into fully functioning neurons when subjected to certain in vitro conditions.

Ethical considerations and controversies:

The use of embryonic stem cells (ESCs) in both scientific investigation and medical treatment has engendered substantial ethical deliberation due to their derivation from human embryos. Nevertheless, the use of these cells for medical reasons raises ethical considerations about the potential loss of embryos. Various sources of pluripotent stem cells (PSCs), including adult mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs), have been investigated as potential solutions to these ethical concerns. Sun with his friends [31] have shown evidence of the existence of a distinct population of adult stem cells known as Very Small Embryonic-Like Stem Cells (VSELs), which possess the capability to undergo differentiation into cardiomyocytes.

2.1.2. Adult stem cells (ASCs)

Sources and isolation methods:

Mesenchymal stem/stromal cells (MSCs), another name for adult stem cells, may be extracted from many parts of the body. Adipose tissue is a frequent source of stem cells made from ASCs (adipose-derived stem cells). These cells are widely distributed and simple to reach. There are many methods for removing these cells, but collagenase digestion and explanation are the most often used ones. Using these methods, Stage and research group evaluated the ability of horse ASCs isolated from different adipose tissues to differentiate into several lineages. The ability of ASCs to undergo osteogenic and adipogenic differentiation is significantly impacted by the process of tissue localization and dissociation [30].

Further research is being done on human corneal stromal stem cells (CSSCs) to see whether or not they may be used in regenerative medicine. The goal of this effort was to create immortalized CSSC lines from significant human CSSCs in order to get over the restrictions placed on separation methods, donor variability, and cultural lifespan. The immortalized cells had the same morphology, proliferative activity, and capacity for multi-lineage differentiation as the original CSSCs [9].

Differentiation capacity and limitations:

ASCs have been demonstrated to have the ability to differentiate into a variety of distinct cell types. For instance, horse ASCs have shown remarkable chondrogenic, osteogenic, and adipogenic expansion potential. However, Stage's team [30] demonstrated that they were resistant to some cardiomyogenic differentiation inducers. In a separate investigation, it was shown that hPSCs may differentiate into MSCs with therapeutic potential. Reduced cellular senescence, increased cytokine release, successful tri-lineage differentiation, and increased proliferative capacity are all hallmarks of these cells [6].

2.1.3. Induced pluripotent stem cells (iPSCs)

Reprogramming process and applications:

Induced pluripotent stem cells (iPSCs) are characterized by their ability to undergo self-renewal and differentiate into a wide range of cell types. Considerable focus has been directed into the methodology used for the generation of induced pluripotent stem cells (iPSCs), notably within the realm of regenerative biology. Through the use of many transcription factors, it is possible to induce the reprogramming of adult differentiated cells into a pluripotent state. This methodology offers a reservoir of pluripotent cells that may be genetically altered and specialized into certain cell types, potentially

serving various therapeutic purposes. Several studies, notably the one have emphasized the significance of therapeutic research using induced pluripotent stem cells (iPSCs) and CRISPR/Cas9 gene editing technologies [1].

Advantages and challenges:

Patient-specificity is the key benefit of iPSCs since it lowers the likelihood of graft-versus-host disease after transplant. However, concerns regarding their safety after transplantation have been raised due to their immunogenic and tumorigenic properties. The potential use of iPSCs as a promising cancer vaccine in cancer immunotherapy while also noting the limitations involved with efficiently employing iPSCs, including their tendency to induce tumors [23]. Martin [18] highlights further problems, including a poor success rate and inadequate functional integration of cellular transplants.

2.2. Current Applications of Stem Cell Therapy:

2.2.1. Hematopoietic stem cell transplantation (HSCT)

Treatment of blood disorders and malignancies:

Hematopoietic stem cell transplantation (HSCT) has been used for a long time to treat both malignant and non-malignant blood diseases. Systemic sclerosis (SSc) and multiple sclerosis (MS), which together account for around 80% of all instances of autoimmune disease (AD) transplantation, have been treated with autologous hematopoietic stem cell treatment (autologous HSCT) for over 20 years. The European Society for Blood and Marrow Transplantation (EBMT) reports a declining trend in transplant-related mortality, relapse/progression, and progression-free survival over time. These modifications are intrinsically linked to the knowledge and expertise of transplant facilities, the selection of patients, and the facilitation of advancements in treatment. This highlighted the importance of HSCT in the treatment of blood diseases and malignancies in their extensive review of HSCT conducted for ADs between 2015 and 2020 [5].

Successes and limitations:

The use of HSCT has shown promising results in the treatment of neurological illnesses, notably those caused by Inborn Metabolic Errors. Congenital defects in enzymes cause inflammatory demyelination of the brain in diseases like X-linked Adreno-leukodystrophy. The replacement of microglia derived from the hematological system with myeloid precursors generated using allogeneic methods has shown promise in preventing neuronal degeneration. Donor-derived myeloid cells are pivotal in influencing the brain's microclimate and facilitating repair processes like remyelination. However, graft-versus-host disease and slow microglia turnover are still problems in this area [8].

2.2.2. Tissue engineering and organ transplantation

Skin and bone regeneration:

Tissue engineering (TE) is a promising technique for fixing or replacing damaged tissue. The use of peptide self-assembly to fabricate biocompatible three-dimensional tissue constructs is a major advance in this study. Because of their high affinity for extracellular integrin receptors, peptides belonging to the arginine-glycine-aspartic acid (RGD) family have been singled out as a significant ligand. RGD peptides are ideal targets for tissue regeneration, therapy, and organ replacement due to their unique expression patterns in a broad variety of human tissues and relationship with a number of pathophysiological disorders. RGD-based ligands have seen extensive usage in biological studies, particularly those focusing on tissue and organ development. Artificial neovascularization, bone tissue engineering, and corneal healing are just a few examples of how the structure and sequence of RGD peptides are essential to the success of tissue engineering [16].

Bioengineering has allowed for major developments in regenerative medicine, particularly in the domains of oral and craniofacial tissue engineering. The development of bioengineered tissues and other functional structures with the potential to repair and regenerate damaged organs has had a profound effect on the field of medicine. Hydrogels, which contain a high percentage of water, have emerged as one of the most widely used scaffolds in tissue engineering during the last two decades. Their capacity to imitate genuine tissues, bone, and cartilage has made them promising for use in cell immobilization and growth factor application, particularly in dental and osseous tissue engineering [2].

Challenges in creating functional organs:

Despite the rising incidence of cardiac problems around the globe, heart transplantation continues to be the most beneficial alternative. However, challenges like as organ rejection, a dearth of donors, and prohibitive healthcare costs remain. Nanotechnology provides a potential answer, with nanoparticles playing a crucial role in the creation of cardiovascular scaffolds that facilitate simple tissue regeneration. Functional nanofibers have aided in the creation of stem cells and the regeneration of cells and tissues. The nanoscale nature of these materials, however, may make it difficult for them to interact with living organisms due to their small size [3].

Deterioration of tissues and organs due to chronic diseases usually lowers patients' quality of life. Hepatitis, osteoporosis, and Alzheimer's disease are just a few of the disorders that may severely impact an organ's functionality. Despite immunological rejection and disease progress, organ transplantation remains the foundation of treatment. In recent years, AMSC-MP, or metabolites derived from amniotic mesenchymal stem cells, have emerged as a promising new treatment option. These cytokine- and growth factor-containing metabolites have showed promise in regenerative medicine, with several potential pharmacological uses for a wide variety of diseases. However, there are still major issues with mass manufacturing and product availability [20].

The European Society of Cardiology (ESC) Working Group on Cardiovascular Regenerative and Reparative Medicine (CARE) organized a scientific retreat in November 2018 to present and critically debate major research discoveries in regenerative and/or reparative medicine. The objective was to make preparations for the growth of the industry. The conference's talks and conclusions highlighted the potential of stem cells to revolutionize regenerative medicine and the need of an all-encompassing approach to overcoming the obstacles that stand in the way.

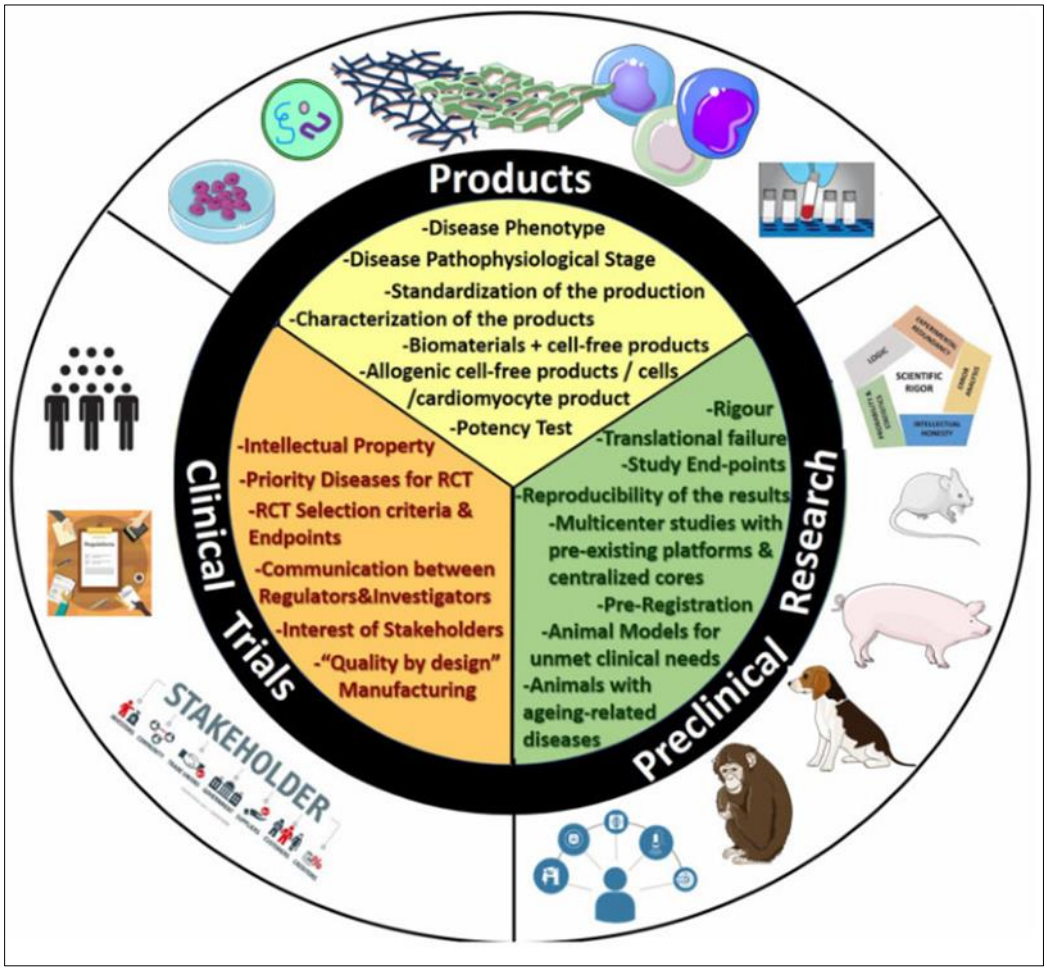

Figure 2 The diagram shows the conceptual priorities in cardiac and regenerative medicine, divided into three main areas: manufacturing, preclinical research, and clinical trials and those areas each of these contains important issues that must be addressed for the successful advancement of stem cell therapy

During product development, the focus is on understanding and managing the disease phenotype and pathophysiological stages to optimize treatment This includes standardizing products to ensure accuracy and quality good in medical manufacturing. In addition, it is important to properly characterize these products to ensure their safety and efficacy. Researchers are also exploring cell-free materials from biomaterials as alternatives to traditional cell-based methods. In particular, the potential of allogeneic cell-free products and cardiac cell therapy is under investigation. A key aspect of this work is the use of robust potency tests to accurately measure the potency of therapeutic agents [30].

Preclinical evaluation emphasizes rigorous testing and repeatability to create a solid foundation for appropriate treatment. Ensuring a high level of scientific rigor is essential to obtain reliable results. Addressing the translational failure that reflects the challenge of translating preclinical success into clinical practice is also a major concern. Defining clear and appropriate endpoints helps measure the success of preclinical studies. Reproducible results are key, so protocols that provide consistent and reproducible results are essential. Multicenter testing with pre-existing platforms and centralized cores helps validate results under different conditions.

Pre-registration before the study begins ensures transparency and reduces publication bias. The use of appropriate animal models that better mimic human heart disease is essential, and the inclusion of older animals in studies helps to understand the effects of treatments at different ages. The clinical trial aspect is critical to the translation of research into practice, requiring careful planning and stakeholder engagement. Intellectual property protection encourages investment and growth in this sector. Identifying priority diseases for randomized controlled trials (RCTs) is important for clinical trial implementation based on efficacy and feasibility. Defining specific criteria for patient selection in addition to trials and defining meaningful endpoints improves the relevance and effectiveness of trials. Effective communication between regulators and investigators streamlines the testing process, making it more efficient. Taking into account the views of all stakeholders, including patients, researchers and health professionals, is essential for comprehensive and inclusive research To adopt a "quality by design" approach emphasizes quality throughout the development process, ensuring that the final medical products meet the highest standards. This diagram and its detailed implications provide an overview of the critical concepts required to improve cardiac regeneration Addressing these critical factors can allow researchers and improved clinical practice and improved clinical use of stem cell therapy, which will ultimately improve patient outcomes in regenerative medicine [12].

2.2.3. Neurological disorders

Parkinson's disease and Alzheimer's disease treatment:

Parkinson's disease (PD) and Alzheimer's disease (AD) are only two of the many neurological diseases that contribute significantly to global mortality and disability. Given the staggering prevalence of these diseases, it's no surprise that effective treatment choices are frequently hard to come by. Cell-based treatments are developing as a viable option in the modern exploration of innovative approaches to treat neurological disorders [14].

Many different neurological illnesses have been shown to respond well to stem cell transplantation therapy. Numerous neurological disorders, including Parkinson's disease (PD) and Alzheimer's disease (AD), may originate from a neuronal or glial cell deficit or injury. Recent advances in cell culture methods have made it possible to create neurons and glial cells in the lab from stem cells. As a result, researchers have been motivated to create transplantation treatments based on stem cells for use in human patients. Brain cells, for example, may either continue to be stem cells or develop into other types of cells. Although there are still obstacles, this cellular advancement may provide a means by which patients might have a more normal existence [25].

In addition, stem cells may be used in a variety of cell therapy applications. When it comes to treating neurological problems, their usage is especially important since there is currently no cure accessible via traditional medicine. Animal models of PD and AD transgenesis have been used to investigate the efficacy of stem cell treatment. There have been some promising and some unsuccessful clinical trials based on promising animal research [35].

Promising results and ongoing research

Transplanting stem cells from one individual to another has great promise, as shown by both preliminary human trials and promising animal models. Stem cell therapy has shown promise as a viable treatment option, particularly for neurological illnesses. Since stem cells have the potential to develop into numerous cell types, including muscle, red blood, and brain cells [25], there is promise for the repair of impaired neural function.

Repurposing drug initiatives to improve the efficacy of cell transplantation therapy for neurological illnesses have also been investigated. Using promising repurposing options to improve cell transplantation treatments might be a useful therapeutic combination [21].

2.2.4. Autoimmune diseases and immunomodulation

Multiple sclerosis and Type 1 diabetes therapies:

Autoimmune diseases are characterized by immune system dysfunction and tissue damage triggered by the body's immunological reaction to self-antigens. Imbalances in immunological homeostasis are often associated with these disorders. Mesenchymal stem cells (MSCs) are a viable therapeutic approach because of their multipotent nature, which allows them to self-renew and specialize into diverse cell types. Both regenerative medicine and immunomodulation benefit greatly from the use of these cells. Multipotent stem cells (MSCs) have the potential to develop into many distinct cell types in culture. MSCs are useful in cell therapy because of their differentiation potential. Multiple sclerosis, type 1 diabetes, and rheumatoid arthritis are among autoimmune disorders that recent studies have shown MSCs to be a beneficial treatment for [15].

The importance of the immune system in fighting against toxic substances was also underlined in a different research. However, autoimmune diseases may occur when the immune system fails to properly identify own cells from foreign invaders. Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus are only a few of the most prevalent autoimmune disorders. Stem cell-based treatments and developments in regenerative medicine have opened the door to novel medicines for numerous autoimmune diseases. This chapter analyzed the numerous kinds of stem cells and treatment approaches for each autoimmune illness, with a particular emphasis on the effectiveness of stem cells in attaining the expected goals [26].

Immune-related risks and safety concerns:

There is promise in stem cell treatments, but they also come with certain dangers. One of the major concerns following a transplant is the potential for immunological responses. If the body rejects the transplanted cells as alien, an immune response might occur. This might lead to a rejection of the transplanted cells or perhaps an autoimmune response. In addition, the transplanted stem cells may promote tumor development, a phenomenon known as tumorigenicity. The safety of the patient and the efficacy of the treatment after a transplant depend on close monitoring of the patient [15].

2.3. Advances in Stem Cell Research:

2.3.1. CRISPR-Cas9 technology in stem cell editing

Gene editing for disease correction:

CRISPR/Cas9 has had a revolutionary impact on genetics and regenerative medicine. This technique has allowed "gene correction," the process of adding normal sequences or removing mutant sequences from precise sites within the genome, a reality. These methods have opened the door to treating genetic disorders that run in families. Induced pluripotent stem cells (iPSCs) isolated from people with genetic diseases provide a promising new avenue for treating these conditions by correcting faulty genes. Autologous organ transplantation might take advantage of the differentiated progeny of these genome-edited iPSCs, such as neurons, hematopoietic cells, and cardiomyocytes. Evidence suggests that iPSCs created from people with diseases like cystic fibrosis and thalassemia may correct genetic flaws [27].

Ethical considerations and safety issues:

Rapid advancements in CRISPR/Cas9 technology have reignited many moral discussions, particularly in religious contexts. There are concerns about interfering with God's creation, violating human dignity, the technology's effectiveness and safety, and the possibility of human genetic development. Concerns concerning the ethical and religious implications of genome editing that might result in inheritable changes to the human genome have prompted additional study of the topic [10]. Furthermore, CRISPR/Cas9 has major ethical and technological constraints, despite its enormous promise. Application of this technique to cardiovascular diseases, for instance, necessitates changing DNA repair processes, enhancing genome editing tool designs, and analyzing the efficiency and safety of these methods [32].

2.3.2. Tissue engineering and organ transplantation

Skin and bone regeneration:

Tissue engineering has allowed for significant progress in the regeneration of skin and bone. Tissue replacements that are both biologically plausible and therapeutically useful are now within reach, thanks to advancements in three-dimensional (3D) bioprinting technology. Integrating the complex circulatory networks required for waste disposal and nutrition delivery is the primary problem of preserving the viability of 3D printed tissue. Improvements in the inclusion of these circulatory networks into 3D printed tissues have been made recently to open the way for more efficient skin and bone regeneration operations [7].

Challenges in creating functional organs:

However, there are still challenges to be overcome before 3D bioprinting can reliably manufacture complex tissue structures and completely functioning replacement organs. One of the most difficult problems is creating organ-specific cancer organoids that faithfully reproduce the pathophysiological aspects of spontaneous carcinogenesis and metastasis. Predictive biomarker identification, individualized therapy strategies, and pharmacological screening for a specific patient all rely on the use of organoids. Combining cancer organoids with other technologies, such as organ-on-a-chip and CRISPR-Cas9-mediated transgenesis, may help overcome these constraints and develop more appropriate model systems that imitate the complex stroma of cancer and possible multi-organ metastasis [24].

2.3.3. Small molecules and growth factors for stem cell manipulation

Enhancing stem cell proliferation and differentiation:

Stem cell research has recently made feasible a revolutionary technique that uses small molecule compounds to directly transform one kind of cell into another. Examples include the chemical reprogramming of human fibroblasts into brain cells, Schwann cells, and cardiomyocyte-like cells using a variety of molecular combinations. The potential for employing apical papilla stem cells (SCAP) to generate endothelial cells (ECs) was investigated. The findings proved that SCAP-derived chemically induced endothelial cells (SCAP-ECs) produced endothelium-specific gene and protein upregulation. These SCAP-ECs formed tubular shapes, released nitric oxide (NO), and absorbed acetylated low-density lipoprotein (ac-LDL) in vitro, all hallmarks of endothelial cells. Similar to human umbilical vein endothelial cells (HUVECs), SCAP-ECs migrated and proliferated, and they also helped blood vessels form in vivo when exposed to a pro-inflammatory environment. Yi with his team [33] research suggests that a combination of small molecules and growth factors may considerably improve SCAP endothelial transdifferentiation, making SCAP a practical cell source for vascular engineering and the treatment of ischemic diseases.

Promising approaches and potential risks:

In a separate study, researchers looked at the feasibility of creating cardiomyocytes from pluripotent stem cells in mice. Researchers employed a Mesp1-expressing mouse embryonic stem cell culture that could be induced with doxycycline to successfully differentiate into cardiomyocytes. As part of the cardiac differentiation strategy, we first temporarily activated Mesp1, and then we inhibited the Wnt and TGF signaling pathways using small molecules. The findings showed that simultaneous blockage of both routes resulted in a greater number of cardiomyocytes being produced. Mesp1-induced cardiac development: clarifying the potential interplay of TGF and Wnt signaling pathways, and pointing to a straightforward, low-cost technique of generating mice cardiomyocytes [22].

Another study suggests that little amounts of chemicals may enhance endothelial cell (EC) treatment, resulting to enhanced vascular development or re endothelization in a variety of therapeutic settings. With these findings, Belt and friends propose a feasible technique for the treatment of regeneration EC by showing the role of small compounds in boosting stem cell differentiation and proliferation [4].

2.4. Challenges and Safety Concerns:

2.4.1. Tumorigenicity and teratoma formation

Human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) are two examples of pluripotent stem cells that have demonstrated promising results in stem cell treatment. However, when injected into humans, these cells may develop into tumors, especially teratomas. Teratomas are malignant tumors that develop from pluripotent stem cells and include tissue from all three germ layers. The development of teratomas has been a major roadblock to the

therapeutic use of iPSCs and hESCs. Recent genomic studies have emphasized the genetic and epigenetic anomalies associated with induced pluripotency, highlighting the tumorigenic potential of these cells [11].

2.4.2. Immune rejection and immunogenicity

Stem cell therapies, particularly those using pluripotent stem cells like induced pluripotent stem cells (iPSCs) and human embryonic stem cells (hESCs), have shown therapeutic promise. However, transplanting these cells into patients has the potential to cause malignancies, especially teratomas. Cancerous teratomas arise from pluripotent stem cells and include cells from all three germ layers. The formation of teratomas has been a major roadblock in the therapeutic use of hESCs and iPSCs. Recent genomic studies have highlighted the genetic and epigenetic abnormalities connected to induced pluripotency [11], highlighting the potential tumorigenicity of these cells.

2.4.3. Ethical considerations and public perception

The use of stem cells, in particular hESCs, has presented several moral challenges. Since pre-implantation embryos are the source of hESCs, debates regarding the morality of embryos have arisen. An alternative to hESCs was made possible by the development of iPSCs, potentially resolving ethical issues. Nonetheless, new moral conundrums have been brought forth by the reprogramming procedure and the potential for genetic modifications. Furthermore, the public's perception of stem cell research and therapy is influenced by both the prospective benefits and the related ethical issues. To guarantee the successful clinical translation of stem cell treatment, it is essential to address these difficulties and maintain open communication.

2.5. Future Directions in Regenerative Medicine

2.5.1. Personalized medicine and patient-specific therapies

The advancement of space travel and the availability of low Earth orbit (LEO) habitats like the International Space Station (ISS), operated by the United States National Laboratory, have made it possible to perform R&D operations in ways that would be impossible on Earth. The LEO environment has several benefits for life science research, one of the most notable being the capacity to perform experiments in conditions with permanent microgravity. This one-of-a-kind environment has enabled groundbreaking studies in tissue engineering and regenerative medicine, notably in the areas of stem cell proliferation, differentiation, biofabrication, and disease modeling utilizing microphysiological systems (MPS). Both our grasp of biology and the pace at which medical technology and healthcare have advanced have benefited from these kinds of investigations. As a result of these advantages, biological study in LEO may provide results that are impossible to get on Earth [16].

2.5.2. Advancements in tissue engineering and regenerative scaffolds

Additionally, Government-funded fundamental research is becoming less important than commercially financed R&D with terrestrial applications, which is creating a healthy environment for LEO production and innovation. This change emphasizes how important it is to have finance and public-private partnerships in order to promote essential research and development that makes use of the benefits of the LEO environment. The potential economic value and benefits of space-based biomanufacturing to life on Earth have been highlighted by recent ISS research. This involves combining biological and non-biological components to produce biomolecules and biomaterials that are marketable and may be used for preclinical to therapeutic applications.

2.5.3. Stem cell banking and its implications

The continuous existence of the ISS in Low-Earth orbit provides a useful platform from which to promote the ISS's positive effects on Earth's economy. To bridge the gap between the early stages of space-based biomedical research and the establishment of a sustainable, investment-worthy biomanufacturing market in LEO supported by future commercial platforms, the ISS National Lab's provision of access to the space station is crucial.

2.5.4. Artificial intelligence in stem cell research and therapy optimization

Many promising areas for future research and development (R&D) in space-based biomanufacturing were highlighted during the Biomanufacturing in Space Symposium. Biofabrication, stem cells and their derivative products, and disease modeling are all viable choices. The need for more research to evaluate and mitigate the risks associated with these prospects was also stressed throughout the meeting. Producing and collecting the necessary data is a prerequisite, and experts agree that automation, AI, and machine learning are crucial. Participants at the seminar recognized the need for public-private collaborations and funds to investigate these possibilities for a manufacturing industry in LEO.

3. Conclusion

Expectations and attention to the field of regenerative and reparative medicine are high, particularly when it comes to cardiovascular diseases like heart failure (HF). Good preclinical results stoked initial enthusiasm and prompted prompt transfers into clinical research. Nevertheless, the disappointing results of these clinical investigations imply that the preclinical evaluations could not have been comprehensive enough to forecast clinical outcomes. Several barriers have been found to prevent these medications from being used in clinical settings including varying biological products, problems in creating tests for quality and potency, insufficient rigor in preclinical research and issues with reproducibility and problems in manufacturing.Over the last several years, claims of scientific oddities have surfaced. The clinical acceptability of stem cell and gene therapy products has been called into question due to the absence of expected therapeutic breakthroughs. Funding agencies, industry actors, and physicians are all pessimistic. Some of the most active research groups in the field of cardiovascular regenerative and reparative medicine have been prompted by the current situation to re-evaluate the position and direction of the field. This paper is very helpful to provide a detailed view and information of stem cells, their role in regeneration and dealing with neurological disorders. It gives extensive information about the role of CRISPR-Cas9 and various stem cell therapies for future.

Future challenges and areas for further research and development

The field of regenerative medicine is very new, especially when it comes to using stem cells. Although there is a lot of potential, there are also a lot of challenges that need to be solved. These challenges range from ethical and public perception issues to technical and scientific roadblocks. How well these problems are resolved and how past experiences are integrated into new research and development endeavors will define the field's future.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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