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(REVIEW ARTICLE)

Recent advances in stem cell therapy: Translational applications in regenerative medicine

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Abstract

Stem cell research represents one of the most transformative fields in modern biomedical science, offering groundbreaking potential in regenerative medicine and disease treatment. Stem cells possess unique self-renewal and differentiation capabilities, allowing them to replace damaged or diseased cells in tissues and organs. Various types of stem cells embryonic, mesenchymal, hematopoietic, neural, induced pluripotent, and tissue-resident play crucial roles in tissue regeneration and therapy development. Their applications span a wide range of medical disciplines, including cardiovascular, neurological, endocrine, metabolic, hepatic, renal, and cancer-related disorders. advances have integrated stem cell technology with innovative approaches such as gene editing (CRISPR-Cas9), organoid formation, and biomaterial scaffolds, significantly enhancing therapeutic precision and clinical translation. Stem cell-based therapies are currently being evaluated in numerous clinical trials for conditions like Parkinson's disease, diabetes, myocardial infarction, and spinal cord injuries. Moreover, the development of Advanced Therapy Medicinal Products (ATMPs) has provided structured pathways for using gene, cell, and tissue-engineered drugs derived from stem cells.Despite these promising developments, several limitations persist, including tumorigenicity risks, immune rejection, reproducibility challenges, high production costs, and ethical issues, particularly regarding embryonic stem cells. Addressing these barriers through standardized procedures, genetic screening, and ethical frameworks remains essential for clinical success.Looking forward, stem cells are expected to play a pivotal role in personalized medicine by enabling patient-specific therapies tailored to genetic and environmental factors. Collaborative research models, such as the Triple Helix approach linking academia, industry, and government, are vital to accelerating innovation. Overall, stem cell therapy stands as a cornerstone for next-generation medical treatments, holding immense promise for restoring health and improving quality of life worldwide.

Keywords: Stem Cells;Regenerative Medicine; Organoids; Personalized Medicine

1. Introduction

If we consider the human body as a building, stem cells are the foundation of this building. They are the only cells that have the ability to produce and create specialized cells and can make more than 200 specialized cells such as blood, bone and muscle cells . These cells are produced by the bone marrow. Initially, one type of stem cell builds the body [1].

Then, a different subset of these cells supports these structures by functioning as a maintenance and repair team. The stages and processes of development that take place during the embryonic period, the replacement of damaged cells in the body following illness, and the restoration of normal function of tissues and organs in the body following various injuries are all being better understood by researchers working in the field of stem cells.The direct use of stem cells in

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the treatment of numerous diseases has also been contemplated, and in the many studies carried out in this field, the beneficial effects of this approach have been identified in a number of diseases. This knowledge will be very effective in the discovery of new therapies using cells. Different kinds of stem cells exist. The most adaptable stem cells are embryonic ones. since they have the capacity to evolve into every cell in a growing foetus[2.]

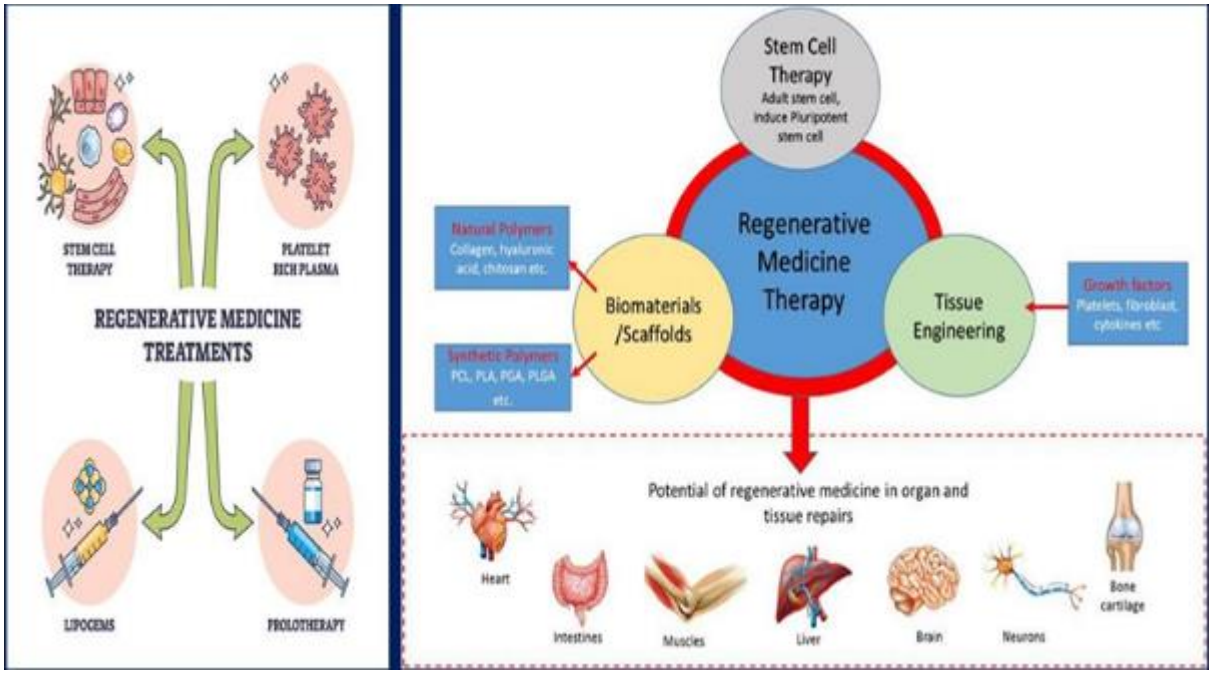

Figure 1 Advances in Stem Cell Therapy for Regenerative Medicine

The majority of stem cells in the body may only aid in maintaining and repairing the tissues and organs in which they reside since they have a limited capacity to produce new cells. Based on their location and function, stem cells can be categorized. Differentiation can also be used to categorize stem cells. Both pluripotent and unipotent stem cells are present under these circumstances. The same embryonic stem cells that can differentiate into any kind of cell or tissue are known as pluripotent stem cells. Embryonic stem cells are obtained by medical researchers from either in vitro fertilization embryos or donated umbilical cord blood. Tissue-specific stem cells can also be unipotent or multipotent cells. Only the tissue in which these cells reside has the ability to produce new stem cells. Adult and embryonic stem cells would be the two primary groups if we were to group stem cells according to where they came from. The same cells that may develop into any type of cell are known as embryonic stem cells, and they are taken from fetal tissue. They have the potential to develop into a fully formed, differentiated embryo. Advanced Therapy Medicinal Products (ATMPs) are defined in order to do this. ATMPs are medical and therapeutic products utilized in humans that are derived from genes, tissues, and cells. The four categories into which ATMP goods are separated are:1. Gene therapy medications: These medications contain genes that have diagnostic, therapeutic, or preventative properties. These products are primarily used to treat a variety of illnesses, such as cancer, chronic diseases, and genetic anomalies, by introducing recombinant genes into the patient's body. In reality, a recombinant gene is a synthetic DNA fragment created in a lab that combines one or more gene fragments from various sources.

2. Drugs used in cell therapy: These include tissues and cells that have been altered to alter their biological properties or that have been utilized for reasons other than those for which they were designed. Additionally, these medications can be used to diagnose, treat, and prevent illnesses .3. Tissue engineering medications: these comprise tissues and cells that have been altered to replace, repair, and regenerate human tissues. . Combination medications: they comprise a biological medication in addition to additional substances and materials. Cells implanted in a biodegradable substrate or scaffold serve as a common illustration of this kind of medication [3].

2. Types and Sources of Stem Cells

- Embryonic stem cells (ESCs)
- Mesenchymal stem cells (MSCs)
- Hematopoietic stem cells (HSCs)

- Neural stem cells (NSCs)
- Induced pluripotent stem cells (iPSCs)
- Perinatal/cord blood/amniotic stem cells
- Tissue-resident/adult stem cells

2.1. Embryonic stem cells (ESCs)

In stem cell biology, ESCs have traits that set them apart from one another. They are particularly versatile and have a lot of therapeutic potential due to their pluripotency, which is characterized by unique characteristics that allow them to develop into any human body cell. Furthermore, ESCs have a remarkable capacity for self-renewal, which helps explain why they remain active and effective for long stretches of time. Nonhuman apes, humans, and mice are all possible origins of ESC. Prior to implantation, they are separated from the inner cell mass of the blastocysts. They can generate different types of cells from foetuses and adults both in vitro and in vivo since they are pluripotent cells [4].

2.2. Mesenchymal stem cell

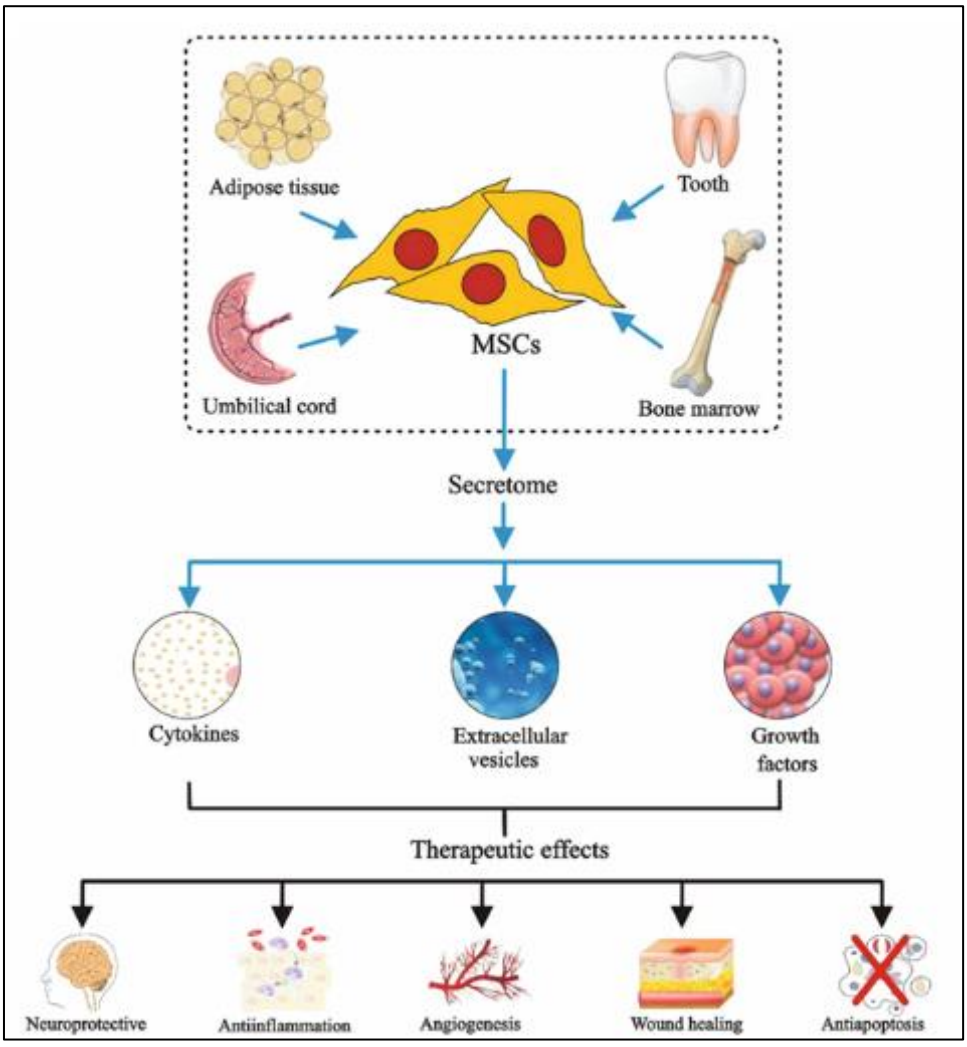

Figure 2 Sources, secretome composition, and therapeutic benefits of MSCs in neuroprotection, wound healing, angiogenesis, inflammation control, and apoptosis prevention

Friedenstein and associates first identified MSCs as multipotent stem cells in the late 1960s . MSCs are non-hematopoietic cells that can differentiate into a variety of lineages, such as ectodermal (neurocytes), endodermal (hepatocytes), and mesodermal (adipocytes, osteocytes, and chondrocytes). Initially, MSCs were believed to be "stromal" cells rather thanstem cells

Multilineage differentiation, immunomodulation, angiogenesis, anti-apoptotic and anti-fibrotic activity, chemo-attraction, and tissue repair development are just a few of the biological functions that MSCs have demonstrated over the past few decades . Furthermore, a range of bioactive substances, such as proteins, growth factors, chemokines, microRNAs (miRNAs), and cytokines, can be released by MSCs, indicating their potential for use [5].

2.3. Hematopoietic stem cell therapy (HSCT)

HSCT has been used to treat multiple sclerosis in clinical trials. Multiple sclerosis is an autoimmune disease that affects the central nervous system. For multiple sclerosis, disease-modifying therapy (DMT) is the standard of care. DMT targets the immune system via changing immune cell trafficking, reducing the number of immune cells, or changing the immune system itself. However, it needs to be used for a long time, and there could be serious side effects. In clinical trials, HSCT has demonstrated more advantages than DMT. [6]

2.4. Neural stem cell biology

NSCs originate in the central nervous system (CNS), where two distinct areas—also referred to as "neurogenic niches"—give rise to NSCs. In adults and developing CNS, these cells are immature.Mature neurons, microglia, endothelial cells, ependymal cells, progenitor cells, and astrocytes are the main biological constituents of adult neurogenic niches. The brain's two main neurogenic niches are the hippocampal sub granular zone (SGZ) and the subventricular zone (SVZ). NSCs are found in the lateral ventricle wall of the hippocampus's dentate gyrus, which is home to the SGZ. Only glial cells can be produced in the other parts of the brain if these neurogenic niches are excluded. Striatum, Optic nerve, Septum, Spinal cord, and neocortex are non-neurogenic areas of the brain. Proliferating cells may be isolated from these areas and, surprisingly, when grafted into the recipient's neurogenic areas, they can produce neurons both in vitro and in vivo[7].

2.5. Induced pluripotent stem cells (iPSCs)

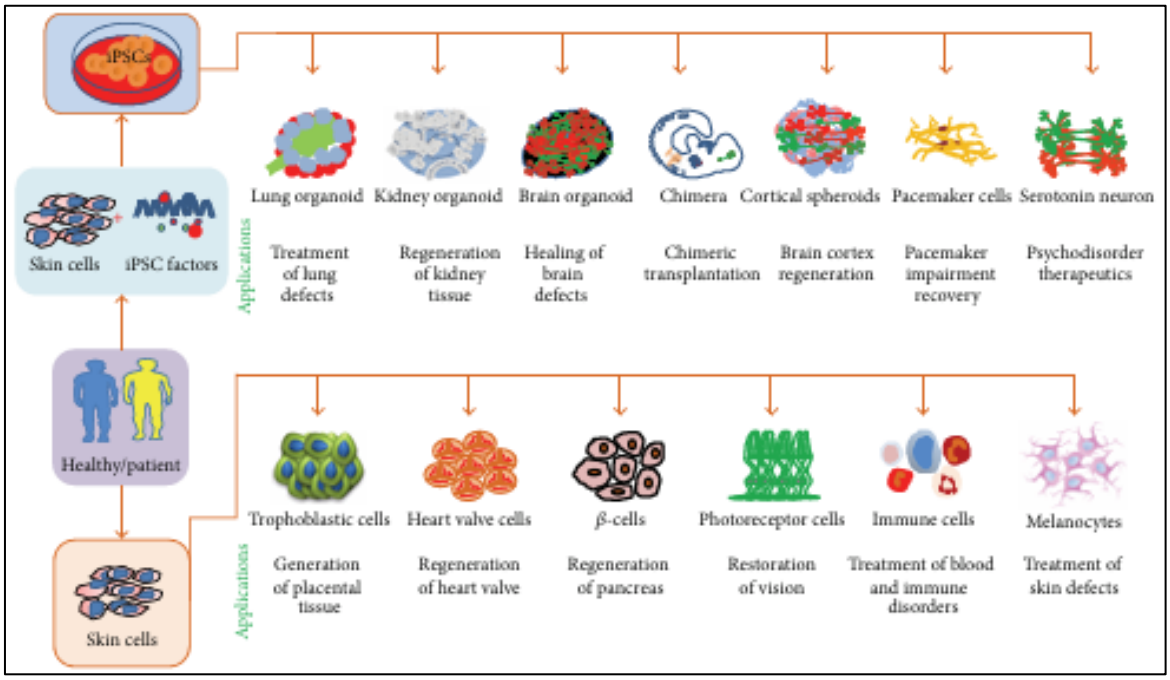

Figure 3 iPSCs in regenerative medicine showing how adult cells can be reprogrammed into ESC-like cells and differentiated into various tissues and organoids for therapeutic use

Since Takahashi and Yamanaka created ESC-like cells in 2006 by genetically incorporating four factors—Sox2, Oct3/4, Klf4, and c-Myc—into skin fibroblasts, the field of iPSC technology and study is fresh compared to all other stem cell studies. Because of their transcriptome profiling, epigenetic markers, and functional competency, produced iPSCs may be distinguished from ESCs due to substantial nuclear reprogramming; nevertheless, the technique of iPSCs has been called into doubt by the use of retroviruses in trans differentiation. The production of iPSCs from several types of adult cells phasing through ESCs or direct trans differentiation has been made possible by technological advancements. The most recent developments in iPSC technology and regenerative applications are described in this review section (Figure 2). Terminally differentiated skin cells can be directly converted into kidney organoids using the latest advancements

in iPSC technology. These organoids share structural and functional similarities with kidney tissue found in vivo. Kidneys may mend themselves to a limited degree, but serious injuries cannot be healed by their natural regeneration potential. A progenitor stem cell must differentiate into 20 different cell types during the kidney's healing process in order to be used for waste removal, pH control, and the replenishment of water and electrolytic ions. The process for producing kidney organoids with functional nephrons in vivo has been discovered for humans. The anatomy and function of this ex vivo kidney organoids are comparable to those of the kidneys in the first trimester of pregnancy. These kidney organoids can be used as models for organ transplantation, disease modelling, and medication nephrotoxicity screening. However, using today's scientific technologies, the creation of fully working kidneys is a distant event. Although safety issues may restrict the use of iPSCs in transplantation, they represent underutilized potential for therapeutic development in pharmaceutical companies and clinical research labs. In conclusion, iPSCs are a safe and efficient way to treat regenerative medicine conditions[8].

2.6. Tissue-resident/adult stem cells

The discovery of adult stem/progenitor cells in the majority of mammalian organisms' tissues and organs has sparked a lot of interest and excitement for their application in cellular and tissue engineering therapies. These cells perform vital roles in homeostatic maintenance by repopulating the mature cell types in the tissues in which they live throughout their lives. The development of adult stem cells' and their early progenitors' functional characteristics both in vitro and in vivo has also shown that, in pathological circumstances, they can actively contribute to the replenishment of mature cell types within the tissue from which they originated. Within the defined niches in each tissue or organ, tissue-resident adult stem cells typically colocalize with supportive cells.BM-derived stem cells (BMSCs), which include hematopoietic stem cells (HSCs), endothelial progenitor cells (EPCs), MSCs, cardiac stem cells (CSCs), and neural stem cells (NSCs) localized in the heart and brain, respectively, are among the well-characterized adult stem cells that have already been shown to be effective in treating certain genetic, hematopoietic, cardiovascular, and/or degenerative disorders in humans[9].

3. Translational Applications in Regenerative Medicine

Table 1 Applications of stem cells

Stem cell applications	Description
Growing new cells in the laboratory to replace damaged organs or tissues	Stem cells can help grow new cells or tissues, which can be used to treat damage and failure of organs such as the liver or heart.
Repairing parts of organs that are not working properly	Stem cells are able to enter and improve the function of failing organs, such as the heart or kidneys.
Investigating the causes of genetic defects in cells	Stem cell research can help identify the causes and factors of genetic defects and provide ways to treat or prevent these problems.
Researching how various diseases, especially cancers, develop	Stem cells are used to gain a better understanding of the cellular and molecular processes that lead to various diseases, especially cancer.
Treating cancers, various malignancies, treating various anemias, and various metabolic diseases	Stem cells are used in bone marrow transplants and other cell-based therapies to fight cancer and blood and metabolic disorders.
Testing new drugs for their safety and effectiveness	Stem cells are used in drug trials to test the efficacy and safety of new drugs before they are marketed and used clinically.

3.1. Stem cell production in a new way

The UK Stem Cell Bank is testing automated robotic technology to cultivate stem cells, according to a March 2023 announcement from the Medicines and Healthcare Products Regulatory Agency (MHRA). The UK is just the second nation to test this technology, according to UK Health and Social Care Secretary Steve Barclay. The robot's ability to produce stem cells will be evaluated over a 12-month period. Since cell-based medicines are frequently exceedingly difficult to generate, their availability has historically been limited, according to Mark Bailey, chief scientific officer at

the MHRA. For instance, despite their high manufacturing costs, contamination, and mass production constraints, human mesenchymal stem cells (hMPC) are the most promising multipotent stem cells for medical use.The development of a novel stem cell robot, which the UK Stem Cell Bank is testing, might alter this and simplify the manufacturing process because it has the ability to lower human error and generate a more reliable final product, Bailey continued. In the end, this might result in Parkinson's disease and other illnesses being treated in a safer and more efficient manner [10].

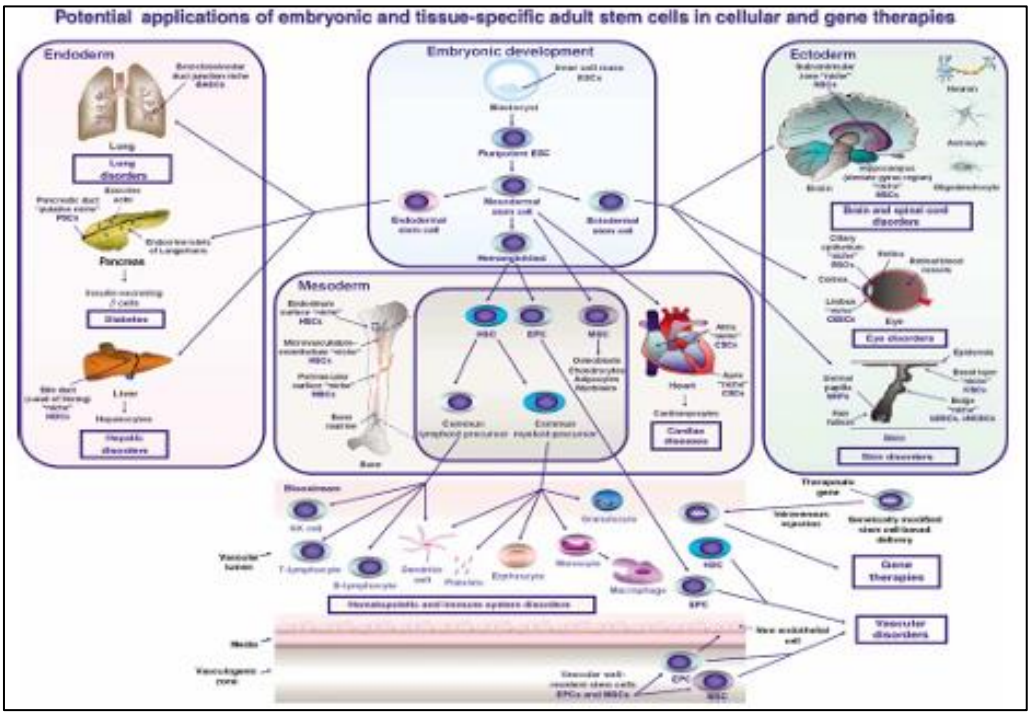

Figure 4 Potential applications of embryonic and tissue- specific adult stem cells in gene cellular and gene therapies

3.2. Cardiac stem cells and their therapeutic applications in cardiovascular diseases

The heart's apex and atria serve as the home locations for cardiac stem/progenitor cells (CSCs), which can differentiate into the three main myocardial cell types—cardiomyocytes, smooth muscles, and vascular endothelial cells—under both healthy and diseased circumstances. Despite the great clinical interest in using these various stem cell types to treat cardiovascular diseases, more research is needed to determine the precise biomarkers and functional characteristics of transplanted cells as well as the molecular mechanisms underlying the effects seen in both in vivo and clinical settings in animal models. Further research is also necessary to determine the specific therapeutic potential of cell delivery techniques, potential interactions between cardiac cell replacement therapies and existing pharmacotherapies used to treat heart diseases in the clinic, and their long-term therapeutic potential. Prior to the potential use of CSCs as safe, effective cellular or gene treatments for cardiovascular disorders in humans, these future studies are required[11].

3.3. Neurological Disorders (Parkinson's, Alzheimer's, SCI, stroke)

Due to limited central nervous system (CNS) regeneration, neurological deficits are usually regarded as irreversible. Compared to other ailments, neurological disorders have a smaller selection of available therapy options. The idea that brain cells cannot regenerate has been called into question by evidence from the migration of brain stem cells in animal models and newly generated neurons in the adult human hippocampal region . The aforementioned discoveries have raised hopes for the possibility of foreign stem cell sources to improve or replenish the brain's stem cell population, especially in relation to neurological disorders. Additionally, the brain and spinal cord's impaired ability to regenerate itself hinders the effectiveness of traditional treatments for neurodegenerative diseases such autism, stroke, cerebral palsy, and spinal cord injury (SCI). Since current treatments are unable to stop the progression of these problems, research has been done all over the world to examine cell-based therapies, including the use of MSCs, as a possible treatment for neurodegenerative diseases. Therapeutic cells must go to the injured regions of the brain to replace, repair, or at the very least halt the degenerative effects of neuronal damage in order for stem cell therapy to effectively cure brain illnesses [12].

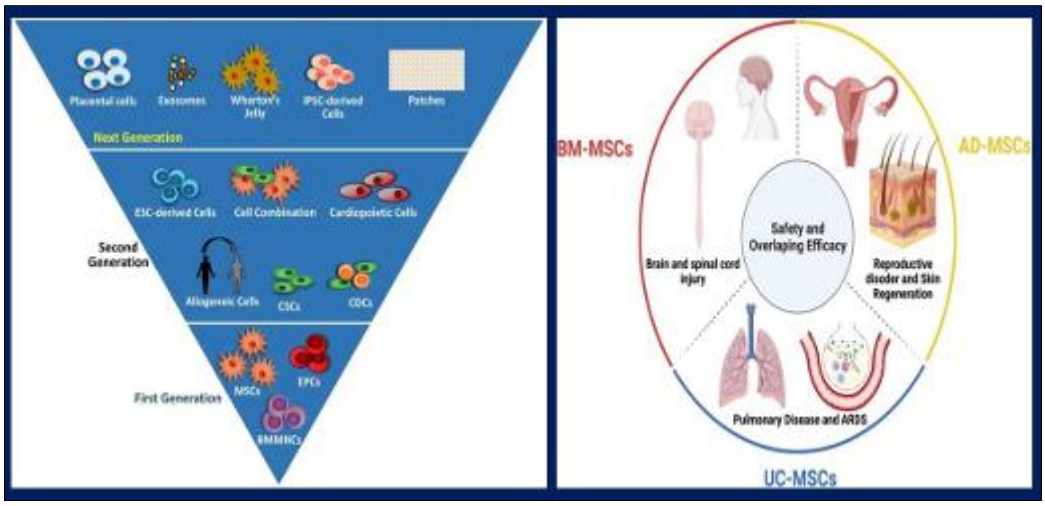

Figure 5 Stem Cell Therapy for Difficult Diseases

3.4. Endocrine disorders

The pathophysiology of several metabolic disorders, such as diabetes, growth problems, thyroid diseases, sexual dysfunction, and reproductive dysfunction, is significantly influenced by endocrine system dysregulation . The fundamental idea behind regenerative medicine is the use of adult stem cells as a template for the regeneration of organs and tissues. Growth factors, hormones, cytokines, and nervous system microenvironmental stimuli (rapid reaction) are examples of endocrine signals. An imbalance in tissue regeneration and homeostasis brought on by disruption of these complex networks can lead to the development of endocrine illnesses in humans, such as diabetes, Asherman syndrome, premature ovarian failure (POF), and sexual hormone deficit .Obesity and diabetes, particularly type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM), have been the biggest challenges in endocrinology research in recent years. MSCs are being researched as a possible treatment approach to address these problems [13].

3.5. Metabolic disorders

3.5.1. Infertility

Infertility, which is defined as the inability to conceive after more than a year of unprotected sexual activity, is an increasing problem in modern society . Numerous illnesses, including POF, endometrial dysfunction, nonobstructive azoospermia, and Asherman syndrome, are linked to infertility. Preclinical research on stem cell-based treatments for restoring reproductive function has lately showed promise. For those suffering from infertility and reproductive disorders, recent research on MSCs presents encouraging opportunities . When autologous BM-MSCs were used to examine two women with POF, the size of the treated ovaries and initial estro gen levels increased, and menopausal symptoms improved [14].

3.6. Cancer & Stem Cells

Stem cells are undifferentiated cells that have the capacity to differentiate into more specialized cell types. Through cell division, they can regenerate themselves. Numerous kinds of stem cells can be produced, and each has special qualities such as self-renewal, unspecialized nature, and differentiation potential . Stem cells show great promise in cancer treatment and regenerative medicine because of their capacity to self-renew and specialize in a variety of cell types, which allows them to treat a wide range of illnesses. Drugs can be delivered directly to the afflicted area and therapy effectiveness can be increased with engineered stem cells .To target and eradicate cancer, stem cells can be used to produce T cells and NK cells . Treatment for cancer The use of stem cell therapy in cancer treatment is a delicate topic that requires careful consideration. Three cell-based therapies—autologous HSCTs, stromal vascular fraction (SVF), and multipotent stem cells, like MSCs—were generally used in untested stem cell clinics to treat cancer. Allogeneic HSCTs provide the capacity to produce donor lymphocytes that aid in the repression and regression of some solid tumours and haematological malignancies; this phenomenon is referred to as "graft-versus-tumour effects."[15]

3.7. Liver regeneration

The liver has an amazing ability to regenerate when injured, but in extreme situations, this ability is insufficient, and hepatic injury may develop into end-stage disease and liver failure. For patients with end-stage liver disorders, such as

acute liver failure and hepatic cirrhosis, orthotopic liver transplantation is presently the only effective treatment. However, its use is severely limited by factors such as waiting list mortality, donor shortage, surgical morbidity and mortality, high expenses, and long-term side effects . Since mature hepatocytes are the most functionally robust cell type for liver cell treatment and have long been acknowledged as the primary contributors to liver healing, hepatocyte transplantation has been proposed as an alternative to liver transplantation.In fact, this strategy has been used in numerous preclinical and clinical studies to treat metabolic and end-stage liver illnesses.Bipotent intrahepatic stem cell (SC) populations—also referred to as resident liver progenitor cells (LPC) in humans or oval cells (OCs) in rodents—emerge and become activated, expand, and actively contribute to the regenerative process by giving rise to hepatocytes and biliary epithelial cells when hepatocyte proliferation is hindered, inadequate, or overpowered by severe liver injury[16].

3.8. Kidney regeneration

Previously, it was thought that bone marrow-derived stem cells could differentiate into renal-resident cells and participate in kidney regeneration following renal ischemia/reperfusion injury.If the damage is not too great and the kidney's structure is unharmed, the kidney still has the capacity to regenerate. Though recent research has indicated that the number of bone marrow-derived cells that engraft injured tubules and develop into functional renal tissue is extremely low, their overall contribution to renal repair would be minimal in the setting of acute kidney injury. Additionally, bone marrow-derived stem cells administered intravenously were found in the kidney and helped to reduce renal fibrosis as chronic renal failure progressed [17].

3.9. Woundhealing

Because they secrete antimicrobial substances, stem cells have antibacterial qualities, aid in immune response regulation, and encourage cell proliferation and differentiation at the wound site. Immune rejection is eliminated when autologous stem cells are used[18]

4. Integration with Emerging Technologies

4.1. Application of organoid technology in RM

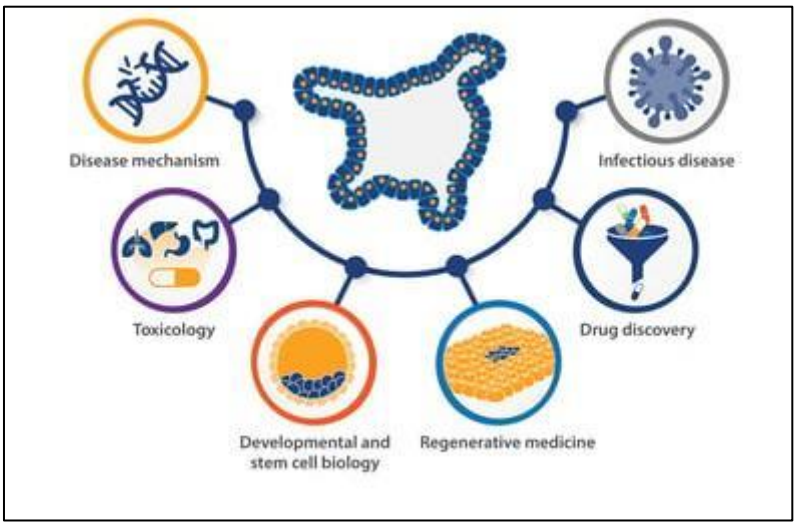

Figure 6 Applications of organoid technology in RM

Organoids are intricate cellular formations in three dimensions that are grouped together to resemble tiny organs. In order to prevent direct physical contact with the dish's bottom, they are cultivated in vitro in suspension cultures. Organoids are stem cell-derived self-organized entities that contain fully differentiated functional cell types that mimic the composition and functionality of natural organs.

By reprogramming differentiated cells or pluripotent embryonic stem cells, organoids can be produced directly from a variety of organs.

In summary, by treating severe, incurable illnesses including diabetes, stroke, paralysis, and MI, RM could save millions of lives[19].

4.2. Gene editing and CRISPR-Cas9

Gene editing has developed into a powerful tool in molecular biology that enables precise DNA sequence modifications to repair genetic defects, look into the causes of disease, and create new remedies. Among the several technologies, CRISPR-Cas9 has revolutionized the field of gene editing due to its effectiveness, versatility, and ease of use. A natural defence against viral infections is the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) system. CRISPR-Cas9 offers a number of benefits. A wide range of researchers can use it because to its inexpensive cost, outstanding efficiency, and ease of design. Furthermore, its ability to target many genes simultaneously enables sophisticated genetic alterations. Finding the genetic causes of a number of illnesses, such as cancer and neurological diseases, has been made possible thanks in large part to CRISPR-Cas9 [20]

4.3. Biomaterials & scaffolds for in situ regeneration

Because biomaterials with innate biochemical capabilities can directly affect the host immunological response and the recruitment and fate of stem/progenitor cells, choosing the right biomaterial is essential for in situ regeneration. Natural, synthetic, or composite materials can be used to create biomaterials for in situ tissue regeneration applications. Natural biomaterials are made from native tissues and can be whole decellularized native tissue or individual polymeric molecules. FDA-approved polymers with superior biodegradable and biocompatible qualities, including as poly(lactic acid) (PLA), polylactide caprolactone (PCL), and polyglycolide (PGA), can be used to create synthetic biomaterials [21].

5. Clinical Translation and Therapeutics

5.1. Stem-cell clinical trials

Clinical trials for stem-cell therapy are booming, which reflects a growing desire to turn research results from labs into effective treatments. Numerous stem-cell types are presently undergoing clinical trials covering a broad spectrum of medical conditions. Current research aims to ascertain if stem-cell treatments might effectively reduce the symptoms of neurological conditions such Parkinson's, Alzheimer's, and spinal cord injuries. Scientists are looking into the potential of stem cells to promote brain regeneration, heal damaged neurons, and alleviate the symptoms of these debilitating illnesses. The purpose of cardiovascular medicine clinical trials is to assess the potential of stem cells, such as MSCs and progenitor cells, in the treatment of diseases such ischemic heart disease and heart failure. The regenerative potential of stem cells in restoring damaged cardiac tissues and enhancing general heart function was investigated in these investigations. Stem cell-based treatments for cancer treatment are now being researched, with particular attention paid to HSC transplantation (SCT) for the treatment of haematological malignancies. To improve therapy outcomes and reduce side effects, researchers have also looked into possible uses for stem cells in combination with conventional cancer treatments. Additionally, stem cells are being used in orthopaedic and musculoskeletal clinical trials to treat diseases like osteoarthritis and bone abnormalities. MSCs are being researched for their regenerative potential in reestablishing bone and joint health, as they are well-known for their ability to differentiate into bone and cartilage.Furthermore, by regenerating pancreatic beta cells, stem-cell therapies are currently being researched for possible uses in the treatment of diabetes. The use of insulin-producing cells produced from stem cells as transplants to control blood glucose levels in diabetic patients has been studied in clinical trials[22].

5.2. Stem cell-derived gene/cell/tissue-engineering drugs

5.2.1. Gene therapy drugs

Genes that produce therapeutic, preventative, or diagnostic effects are present in these medications. These products are primarily used to treat a variety of illnesses, such as cancer, chronic diseases, and genetic anomalies, by introducing recombinant genes into the patient's body. In the laboratory, a recombinant gene is essentially a synthetic DNA fragment that is created and supplied as a mixture of one or more gene fragments[23].

5.2.2. Cell therapy drugs

These medications include tissues and cells that have been utilized for purposes other than their intended use or that have been altered to alter their biological properties. Additionally, these medications can be used to diagnose, treat, and prevent illnesses [24].

5.2.3. Tissue engineering drugs

These medications contain tissues and cells that have been altered to replace, repair, and regenerate human tissues [25].

6. Challenges and limitations

6.1. Safety & tumorigenicity risks, Immune rejection & immune modulation,Ethical considerations

Despite the enormous potential for regenerative medicine, stem cell treatment has a number of drawbacks. Ethical considerations and awareness of the potential drawbacks must be weighed against the enthusiasm for its potential medical applications. This section examines three primary questions: tumorigenicity, immune responses, and ethical considerations. Cancer is a major issue with stem cell therapy. Pluripotent stem cells (PSCs), which include ESCs and iPSCs, have the ability to develop into any type of cell. However, if differentiation is not properly managed, their self-renewing properties increase the chance of teratoma development. Adult stem cells, such as MSCs and NSCs, can experience genetic and epigenetic alterations during in vitro proliferation that can result in malignant transformation. Researchers have examined a number of strategies to reduce the number of undifferentiated cells, as well as the use of suicide gene systems, like inducible caspase-9, to eradicate proliferating cells after transplantation, as well as genetic and epigenetic screening to find and eliminate abnormal clones. Rejection, inflammation, or transplant failure may result from immunological responses brought on by stem cell-based therapies.Autologous stem cell therapy, which uses self-derived cells to circumvent immunological rejection, can result in inflammatory responses. However, employing donor-derived cells for allogeneic stem cell treatment carries a higher risk of immunological rejection and necessitates the use of immunosuppressive drugs. Depending on inadequate reprogramming or epigenetic memory, iPSC-derived cells may maintain immunogenic markers, however this varies by patient. The development of hypoimmunogenic Marei Stem Cell Research & Therapy Page 21 of 24 stem cell lines by altering major histocompatibility complex (MHC) expression, the removal of immunogenic surface proteins using gene editing techniques like CRISPR-Cas9, and the development of universal donor stem cells through novel immune-evasive engineering are examples of contemporary strategies[26].

6.2. Reproducibility & standardization

For stem cell treatments to fulfil their potential, reproducibility concerns must be resolved and they must be standardized. The advancement of stem cell-based treatments from the lab to the clinical setting has been impeded by issues with reproducibility and standardization; these are fundamental reasons for the continuous challenges in achieving consistent and trustworthy results across various labs and clinical settings. Because even minor adjustments to cell management or experimental methodology can have a significant impact on the results, reproducibility is essential in stem cell research. A number of factors, such as uneven cell source, irregular culture conditions, and differences in the molecular characterisation of stem cells, might lead to reproducibility issues in stem cell research Marei Stem Cell Research & Therapy Page.For stem cell-based treatments to be safe and effective, standardization is just as important as repetition. Standardized methods for stem cell collection, proliferation, differentiation, and quality assurance are essential for the safety and effectiveness of stem cell therapies[27].

6.3. Current limitation

Research on stem cells is currently developing slowly due to a number of problems. These include issues with most stem cell culture, the inefficiency and high cost of conventional 2D culturing methods for culturing stem cells, the inability to replicate the stem cell niche, the loss of differentiation capacity during culturing, the absence of standardized 3D culturing methods, inadequate scale-up methods, and more. When PSCs are injected into the body, they may cause teratomas, which are benign tumours that comprise tissues from all germ layers. Moreover, the body may react immunologically to the influx of stem cells. Thus, it is necessary to design better and more effective remedies[28].

7. Future Perspectives

7.1. Personalized medicine

Stem cells and personalized medicine Stem cells play a key role in the development of personalized medicine, which aims to customize treatment to each patient's unique traits, including genetic, environmental, and lifestyle factors. iPSCs offer a powerful platform for creating disease models from a patient's cells that faithfully represent their genetic heritage. This ability enables more thorough investigations of disease causes at the molecular and cellular levels, leading to more accurate diagnosis and the development of focused treatment plans. the repair of genetic abnormalities linked to illnesses, establishing the foundation for customized treatments that target certain genetic changes in individual

cells.Stem cells play an important role in pharmacogenomics by helping to evaluate each patient's unique medication response. By using patient-derived stem cells in pharmacogenomic research, scientists can learn how a person's genetic makeup affects how they respond to different drugs. A major step toward more targeted and efficient health care techniques, these personalized biomarkers significantly increase the accuracy of disease identification and monitoring[29].

7.2. Interdisciplinary & collaborative research

7.2.1. Triple Helix

The term "Triple Helix" usually refers to the blending of government, business, and academia in order to produce innovation and knowledge. We have included universities, small and medium-sized businesses (SMEs), such as the biotech industry, and large pharmaceutical companies in the Triple Helix in our model presented here (Figure 4). We will demonstrate how the advantages and strengths of each organization can be leveraged to propel the development of therapeutic applications of his[30].

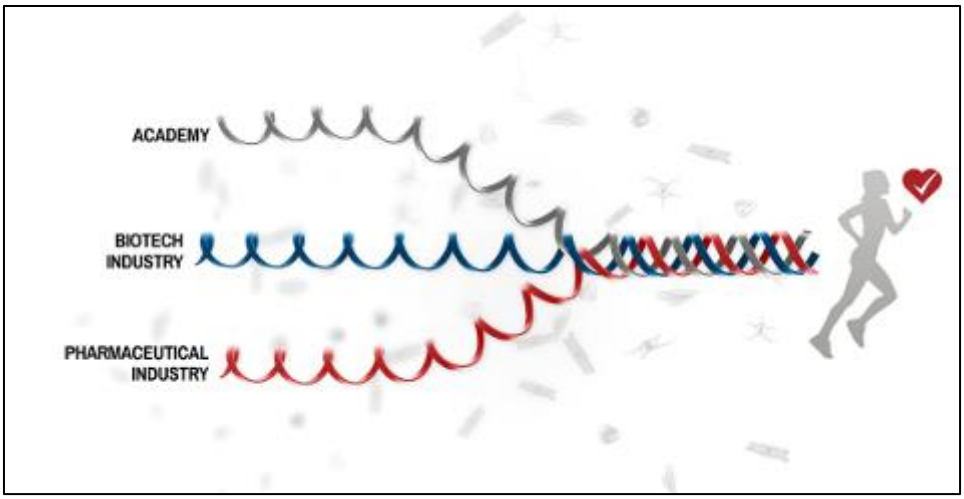

Figure 7 The Triple Helix model showing collaboration between academia, biotech, and pharmaceutical industry to advance regenerative medicine for better human health

7.2.2. ISCT

After more than 20 years of study and development, cell treatments made from induced pluripotent stem cells (iPSCs) are finally being translated into clinical settings. PSC-derived technologies are anticipated to be a major component of the Working Group on Emerging Regenerative Medicine Technologies, which was formed by the International Society for Cell and Gene Therapy (ISCT) in 2022. The Working Group offered recommendations in our earlier review on producing iPSCs that are pluripotent, stable, well-characterized, and appropriate for creating differentiated cell types for allogeneic or autologous cell therapies. These recommendations covered everything from the initial material selection to cell banking [31].

8. Conclusion

Stem cell research holds great promise for the future of medicine. Different types of stem cells, such as embryonic, mesenchymal, hematopoietic, neural, and induced pluripotent stem cells, have shown potential in treating many diseases and repairing damaged tissues. Clinical trials and new technologies like organoids, biomaterials, and gene editing are making these therapies more effective and personalized. However, challenges such as safety risks, immune rejection, high costs, and ethical concerns must still be addressed. With ongoing research and collaboration, stem cell therapy can become a reliable treatment option for many currently incurable conditions, improving health and quality of life worldwide.

Compliance with ethical standards

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Disclosure of conflict of interest

The Author declares that there is no conflict of interest.

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