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Review Article

Stem Cells: Basic Concepts, Methods, Challenges, and Prospects

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Abstract

Stem cells are undifferentiated cells that can self-renew and transform into different cell types. These cells, created during the embryonic period, are found in the body after birth, mainly in places such as bone marrow, fat tissue, and blood. Stem cells play an important role in the regeneration of damaged tissues and are used for therapeutic purposes, especially mesenchymal stem cells. The healing potential of these cells is widely used in the treatment of chronic wounds and orthopedic problems. Unlike muscle cells, blood cells, or nerve cells, which do not reproduce normally, stem cells can reproduce many times. When a stem cell divides, it can become two daughter cells: 1) both can be daughter cells; 2) one stem cell, another different cell; 3) both are different cells. There are two main types of stem cells: embryonic stem cells and developmental stem cells. Stem cell therapy plays an important role in the treatment of many diseases, such as heart diseases, nervous system diseases, and various types of cancer. The regenerative capacity of the root system works by two main mechanisms: asymmetric cell division and stochastic differentiation. In asymmetric division, a stem cell produces a cell similar to itself and a cell that will differentiate. In stochastic differentiation, a stem cell divides into two different daughter cells and creates a new stem cell.

Keywords: stem cell, bone marrow, adipose tissue, cord blood, asymmetric cell, stochastic differentiation

1. Introduction

The ability of stem cells to continuously renew themselves allows them to maintain their populations. These cells can initiate the formation and regeneration of various tissues and organs through differentiation (Figure 1) [1]. In this regard, the article describes the history of development, basic concepts, and classifications of stem cell research and application in medicine [2], [3].

Human pluripotent stem cells (hPSCs) principally consist of embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). Whereas induced pluripotent stem cells are produced by reprogramming differentiated somatic cells, embryonic stem cells come from the inner cell mass of the early embryo. Ectoderm, mesoderm, and endoderm are the three germ layers from which pluripotent stem cells can differentiate [4].

However, adult stem cells are multipotent and or unipotent, and they produce only the cell types appropriate for the specific environment they are living in. The regenerative abilities of stem cells create significant opportunities in cell-based therapies for the repair and replacement of damaged tissues and organs.

Stem cells formation: Embryonic stem cells are formed during the first 4 weeks after fertilization and can differentiate into all cell types. They exist in the blastocyst stage of embryonic development. An important feature of embryonic stem cells is their ability to differentiate into different cell types. However, due to some ethical issues, there are restrictions on the use of medicine. The main application of embryonic stem cells in medicine is due to their significant potential in the regeneration of damaged tissues [5], [6], [7], [8].

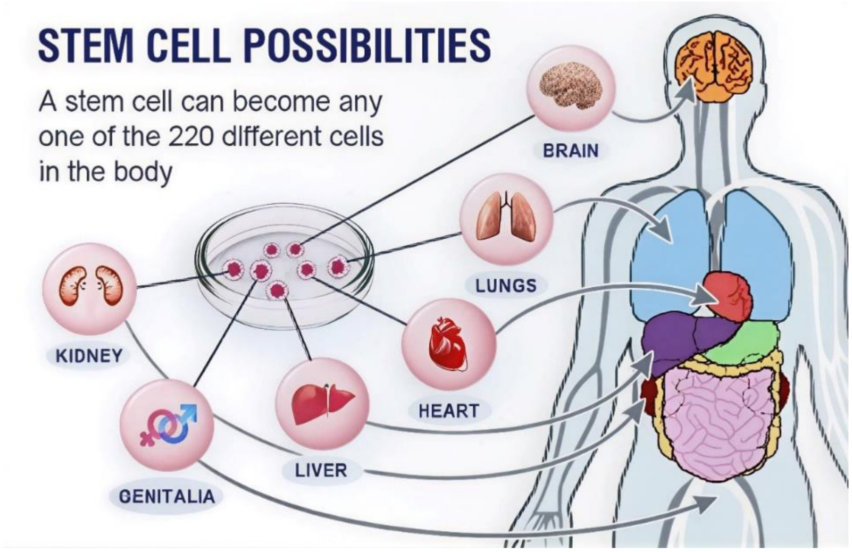

Figure 1. Differentiation of stem cells [1].

Past: The concept of "stem cells" first began with the work of Alexander A. Maksimov in 1909. His early research focused on their development and their main role in disease.

Present: Currently, stem cells are widely used in cancer treatment, regenerative medicine, and pharmacological testing. The induced pluripotent stem cell (iPSC) method allows the development of personalized therapies without raising ethical concerns.

Future: Future applications of innovations such as bioprinting and advanced 3D culture will create new opportunities in tissue engineering and organ replacement. However, challenges remain regarding clinical safety and efficacy [9].

Key stages in stem cell development:

1959 - The first animal (rabbit) was produced by IVF.
1968 - Edwards and Bavister fertilize the first human egg in vitro.
1978 - The first IVF baby is born in England.
1981 - Evans and Kaufman obtain mouse embryonic stem cells.
1996 - Rhesus monkey embryonic stem cells are obtained.
1998 - Thomson and colleagues obtained the first human embryonic stem cell.
2000 - Human embryonic stem cells are shown to be pluripotent.
2001 - United States President Bush approves a limited budget for stem cell research and only allows research using embryos left over from in vitro fertilization [1].
2004 - South Korean scientists clone 30 human embryos and bring them to the blastocyst stage, but only 1 of these embryos can be used to obtain stem cells [1].

2. Ethical Concerns Surrounding Embryonic Stem Cell Research

The main ethical issue in embryonic stem cell research concerns the destruction of human embryos. The moral status of the embryo and whether it is considered a potential human life raises serious questions. Many critics argue that the destruction of embryos is tantamount to the termination of a human life. However, its supporters point out that significant medical advances are possible as a result of such research.

These include the requirement for written consent from donors for embryos resulting from in vitro fertilization (IVF), as well as concerns about the exploitation of vulnerable populations. In addition, discussions about creating embryos solely for research purposes and providing financial compensation to oocyte (egg) donors can raise ethical dilemmas [10].

3. Cultivation and Expansion of Embryonic Stem Cells

Several technologies are used in the cultivation and application of embryonic stem cells:

Cell Culture: Cells obtained from blastocysts are maintained in a specialized nutrient medium for 3-12 months without undergoing differentiation.

Cryopreservation: Stem cells are frozen at low temperatures for long-term storage while preserving their biological characteristics.

Stable Cell Lines: Stem cells derived from human embryos are used to establish stable cell lines capable of indefinite division [11].

Modern technologies include:

Induced Pluripotent Stem Cells (iPSCs): This technology reprograms mature cells into embryonic-like pluripotent cells, reducing ethical concerns and enabling personalized medical applications.

Tissue Engineering: Bioprinting and three-dimensional (3D) culture systems are employed to guide stem cells into forming specific tissues.

Stem Cell Transplantation: The therapeutic use of autologous (self-derived) and donor-derived stem cells is increasingly expanding in the treatment of various diseases [12].

The application of stem cell technology has brought revolutionary advances in the field of regenerative medicine.

Most advanced and effective approaches:

iPSCs: Provide pluripotent cells without the need to destroy embryos, allowing broader clinical and research applications.

Bioprinting: 3D printing techniques allow the formation of tissue-like structures from stem cells, promising breakthroughs in organ repair and replacement.

Tissue Engineering: Enables the restoration of damaged tissues using stem-cell-based biological scaffolds and growth systems [13], [14].

Biotechnological products such as amino acids, hormones, enzymes, and vaccines are widely used to stimulate cell growth and produce biopharmaceuticals. Advances in genetics, molecular biology, microbiology, and enzymology have increased the efficiency of these processes [15].

4. Required Environment for Embryonic Stem Cell Expansion

To prevent embryonic stem cells from differentiating, a special nutrient-rich culture medium is required. The culture medium is regularly supplemented with fibroblast feeder layers, allowing these stem cells to remain undifferentiated for 3-12 months.

Embryonic stem cells are isolated from the inner cell mass of the blastocyst using special enzymatic methods. They can be kept alive for a long time by freezing at extremely low temperatures.

Environmental requirements:

Food composition: The environment should contain some vitamins, amino acids, mineral salts, and sugars that are essential for growth and metabolism.

Oxygen levels: The correct oxygen concentration is important. Thus, a CO_2 concentration of 5-10% and an O_2 concentration of about 21% are considered optimal.

pH: A pH between 7.2 and 7.4 is considered ideal for stem cell culture.

Temperature: The optimal temperature for active cell division and growth of embryonic stem cells is 37°C.

By providing the above conditions, it is possible to store embryonic stem cells for a long time while maintaining their number.

5. Types of Stem Cells

Stem cells are cells that can self-renew and differentiate into other cell types (Table 1). There are three main types:

Totipotent Stem Cells: These cells can develop into all tissues and organs, including both the body (embryonic tissues) and extraembryonic structures such as the placenta. They exist at the earliest stages of embryonic development [16].

Pluripotent Stem Cells: Found from the blastocyst stage of the embryo, these cells can differentiate into almost all cell types of the body, but they cannot form extraembryonic tissues such as the placenta. Embryonic stem cells (ESCs) belong to this group.

Multipotent Stem Cells: These are adult stem cells that can differentiate into a limited range of cell types within a specific tissue or organ. For example, hematopoietic stem cells in bone marrow can produce various types of blood cells. (Figure 2) [17], [18].

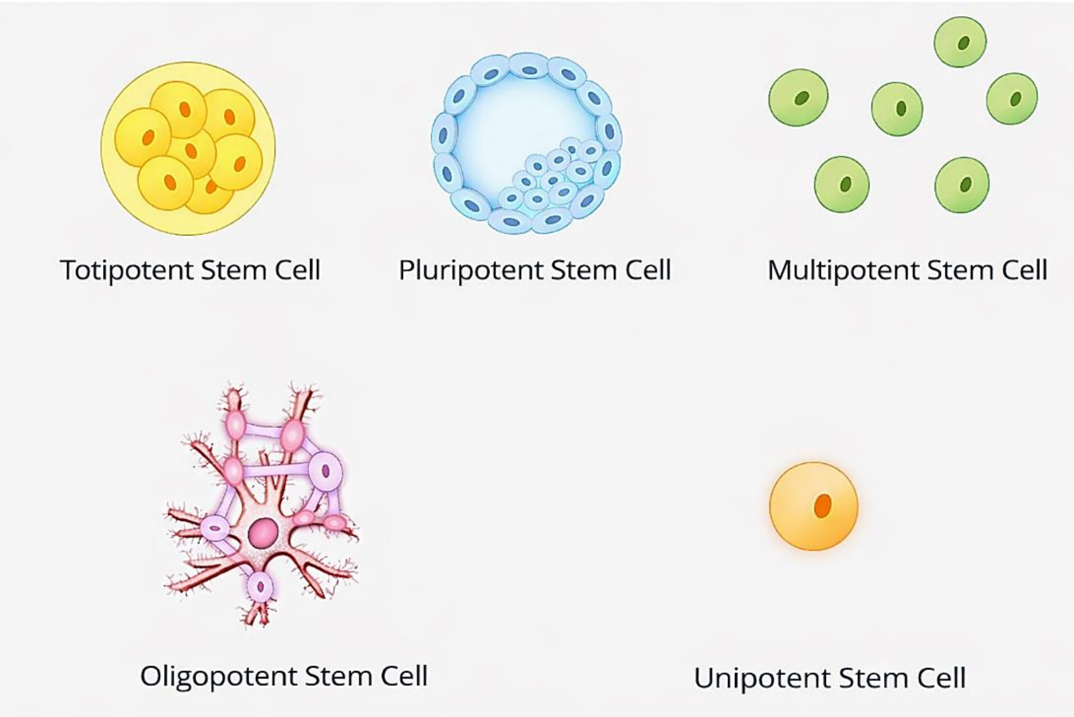

Figure 2. Types of stem cells.

5.1. Totipotent Stem Cells

Totipotent cells are cells that can differentiate into all cell types, including both embryonic tissues (all tissues and organs of the body) and extraembryonic tissues such as the placenta and amniotic fluid. They arise at the very earliest stage of development, beginning from the zygote, and retain their totipotency during the first few cell divisions. Key characteristics of totipotent cells include:

Ability to divide extensively and self-renew.
Capacity to regenerate all tissue types, including support structures needed for embryonic development.
Full synthesis of mRNAs and proteins is required for complete embryonic development.

5.2. Pluripotent Stem Cells

Pluripotent cells are mainly found in the epiblast of early mammalian embryos, particularly during the blastocyst stage. These cells have the potential to differentiate into the three primary germ layers: Ectoderm, Mesoderm, Endoderm, as well as germ (reproductive) cells.

After implantation, the epiblast maintains pluripotency but transitions into a "primed" state in preparation for gastrulation, where lineage specification begins. This pluripotent state is transient and usually lasts only until gastrulation occurs (e.g., in mice, approximately 6.5-9.5 days after fertilization).

5.3. Induced Pluripotent Stem Cells (iPSCs)

Pluripotent stem cells can also be generated from adult tissues using iPSC technology, which reprograms somatic cells (often skin or blood cells) back to a pluripotent state. Steps include:

Cell Collection: Adult cells are obtained through skin biopsy or blood sampling.

Genetic Reprogramming: Key transcription factors (e.g., Oct4, Sox2, Klf4, c-Myc) are introduced using viral or non-viral delivery methods.

Cell Culture: Reprogrammed cells are grown in conditions that maintain pluripotency.

This method avoids ethical issues associated with embryonic stem cell use and enables patient- specific regenerative therapies [10].

Table 1. Difference between totipotent and pluripotent cells.

Feature	Totipotent Cells	Pluripotent Cells
Can form body cells	Yes	Yes
Can form a placenta and extraembryonic tissues	Yes	No
Stage in development	Zygote & early divisions	Inner cell mass of the blastocyst

Pluripotent stem cells are valuable in regenerative medicine**,** especially for repairing damaged tissues and treating diseases such as degenerative disorders and certain cancers.

5.4. Multipotent Stem Cells

Multipotent cells are stem cells present at later developmental stages that can differentiate into a limited range of specialized cell types (Table 2). For example:

"Hematopoietic stem cells" in bone marrow can form all types of blood cells [19], [20].
"Mesenchymal stem cells (MSCs)" can differentiate into bone, cartilage, and muscle cells.

These cells play a key role in repairing damaged tissues in the adult body and are more limited in developmental potential than pluripotent cells [21], [22], [23]. Functional differentiation assays are also used to verify their ability to form specialized cell types.

Table 2. Multipotent stem cells are identified using specific cell surface markers.

Stem Cell Type	Common Markers	Methods Used
Hematopoietic stem cells	CD34, CD45	Flow cytometry, immunocytochemistry
Mesenchymal stem cells	CD73, CD90, CD105	Flow cytometry

Multipotent stem cells are used for:

Tissue repair (e.g., heart tissue regeneration, spinal cord injury treatment).
Immunomodulation (particularly MSCs in autoimmune disease therapy).
Clinical trials for diseases such as myocardial infarction and ALS.

Importantly, they carry a lower risk of tumor formation compared to pluripotent cells.

6. Adult (Somatic) Stem Cells in Aging

In adults, somatic stem cells repair and replace damaged tissues. However, their numbers gradually decrease with age:

In newborns, ~1 in 10,000 cells is a stem cell
In elderly individuals: ~1 in 1,000,000 cells is a stem cell

This decrease causes slower wound healing and reduces regenerative capacity. The following processes can be performed with stem cell-based therapies in older patients: Improve tissue repair, increase functional recovery, and enhance overall quality of life.

The therapeutic effect of stem cells is usually observed within 3-6 months and can last for 6-12 months, depending on the age and health status of the person.

7. Cell Division in Stem Cells

Stem cells are divided into two ways: asymmetric and symmetric.

During asymmetric division, one stem cell and one differentiated (specialized) cell are formed from one stem cell. This allows stem cells to both self-renew and create specific cell types.

During symmetric division, two identical stem cells are produced. In this way, only the number of stem cells increases, but it does not contribute to functional diversity.

Both symmetric and asymmetric divisions are very important for tissue regeneration and development. That is, the main importance of symmetric division is to support tissue regeneration by increasing the number of stem cells. Producing identical copies of stem cells ensures the preservation of the stem cell population, which is very important for the regeneration of damaged tissues. Symmetrical division of stem cells plays an important role in therapeutic applications such as wound healing and tissue regeneration.

The role of asymmetric division of stem cells is to ensure their differentiation into different specialized cell types, which are important for the development and regeneration of the organism. In this way, stem cells maintain their population and at the same time generate new cells with specific functions (Table 3). They allow the formation of various cell types necessary for tissue function. Thus, they contribute to the overall health of the person and the repair of damaged areas.

Table 3. Differences between symmetric and asymmetric stem cell division.

Feature	Symmetric Division	Asymmetric Division
Cell Outcome	Produces two identical stem cells	Produces one stem cell and one differentiated cell
Functional Diversity	Cells share the same function	Cells have different functions
Self-Renewal	Increases the number of stem cells	Maintains self-renewal while supporting differentiation
Role in Development	Promotes tissue growth	Essential for tissue regeneration

8. Diseases Treated with Stem Cells

Stem cells are used to treat the following diseases:

- Cancer (leukemias, lymphomas, brain tumors)
- Bone and cartilage disorders
- Immune deficiency conditions
- Bone marrow diseases
- Hereditary blood disorders
- Metabolic disorders

In addition, stem cell therapy is showing promising results in ongoing research for diseases such as breast cancer, heart disease, and neurological disorders.

The main role of stem cells in treatment is to repair and regenerate damaged tissues. Mesenchymal stem cells are commonly obtained from fat, bone, and cartilage tissues and have the potential to repair damaged tissues in diseases such as arthritis. When stem cells are injected into damaged areas, they stimulate the regeneration process, reduce inflammation, and help form new blood vessels. This method has shown promising outcomes in the treatment of many diseases, including cancer, diabetes, and heart disease (Figure 3) [24].

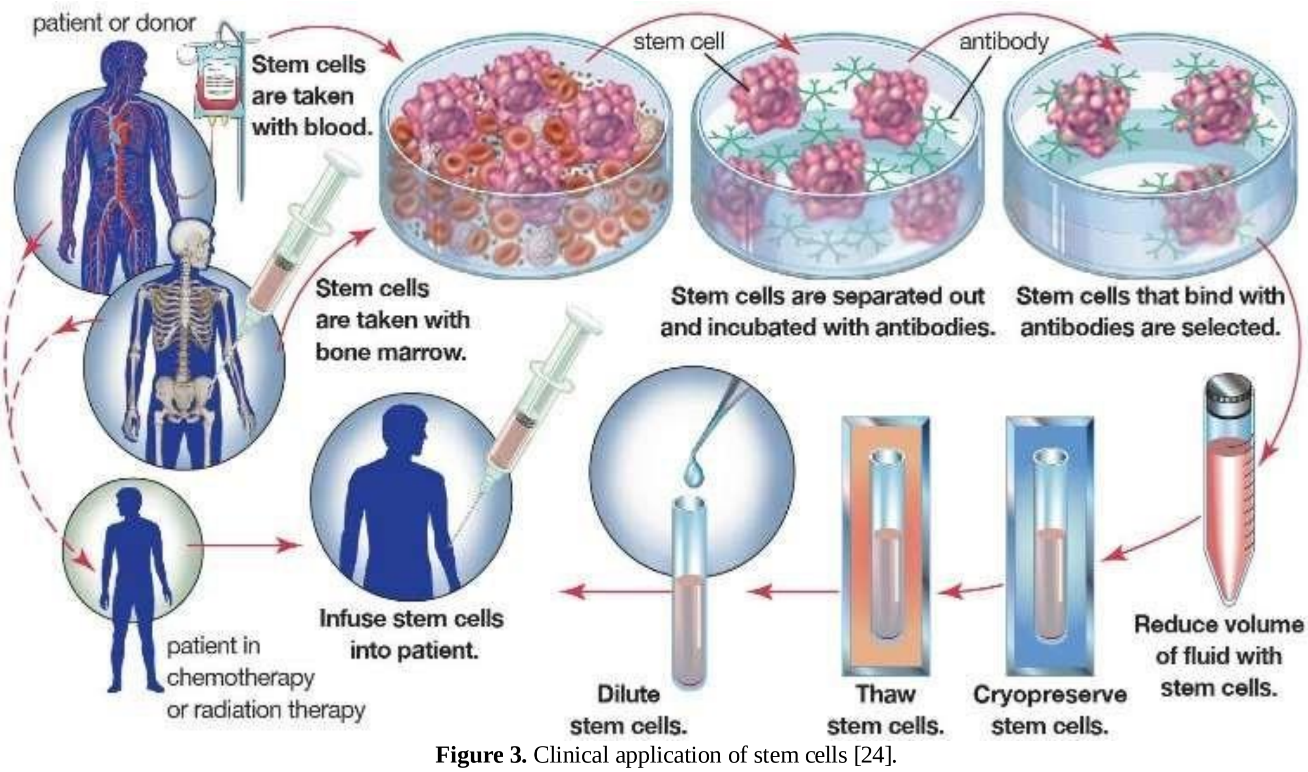

Figure 3. Clinical application of stem cells [24].

The reserve of stem cells depends on age. In newborns, about 1 in every 10,000 cells is a stem cell, but by the age of 65, this ratio drops to about 1 in 1 million. As the body ages, the number of stem cells decreases, making tissue repair more difficult. Stem cells can differentiate into needed cell types and have self-renewal capacity.

Stem cell therapy is commonly used in the treatment of cancer, particularly blood cancer and lymphoma. The therapy usually begins with chemotherapy to destroy cancer cells, followed by the transplantation of healthy stem cells. These stem cells help restore the immune system and play a role in repairing damaged tissues, for example, in heart failure and other conditions. However, there are also several risks associated with stem cell treatment, including cancer.

8.1. Cancer

Stem cell therapy is an effective approach to treating cancer, especially blood cancers and lymphomas. Treatment begins with high-dose chemotherapy, followed by a transplant of healthy stem cells that help restore the immune system. Stem cell therapy accelerates healing by allowing damaged tissues to regenerate. The disadvantage of stem cells is that they can interact with cancer cells and support their spread and growth. Therefore, stem cell therapy should be carried out under very strict medical supervision.

8.2. Bone and Cartilage Diseases

Stem cell therapy is particularly effective in the treatment of cartilage damage. Since they can self-renew and differentiate into different types of tissue, they can stimulate the regeneration of cartilage tissue. Stem cells, especially those derived from adipose tissue, are widely used in the treatment of bone and cartilage damage. Many studies have shown that this therapy accelerates joint healing and reduces pain. The speed and duration of cartilage damage treatment usually vary between 3 and 6 months, depending on the severity of the injury, the effectiveness of the treatment, and the age of the patient. The therapy may be applied in several sessions.

8.3. Immune Deficiency

There are several mechanisms for strengthening the immune system with stem cells:

Tissue repair: Helps repair damaged tissues and supports immune function.

Inflammation reduction: Helps reduce inflammatory processes in the body and increases immune efficiency.

Production of new cells: Strengthens the body's defense system and can transform into various immune cells.

These treatment methods are often used in autoimmune diseases and other immune deficiencies.

Methods used in the treatment of immunodeficiency:

Hematopoietic stem cell transplantation: This method restores the immune system in diseases such as leukemia and lymphoma.

Mesenchymal stem cells: Reduce inflammation and support tissue repair in autoimmune diseases.

Intravenous Infusion and Local Injection: Increases the recovery of damaged tissues.

8.4. Bone Marrow Diseases

Bone marrow diseases are caused by abnormalities in the development of stem cells. Stem cells can differentiate into white blood cells, red blood cells, and platelets. In diseases such as leukemia, aplastic anemia, and myeloproliferative disorders, the bone marrow fails to produce healthy blood cells. Stem Cell therapy helps repair damaged tissue and stimulates the production of normal blood cells.

8.5. Hereditary Blood Disorders

Stem cells also play an important role in the treatment of hereditary blood diseases. Since they can differentiate into several cell types, they can restore blood cell production and support regeneration. This treatment method is very useful in cases where the number of stem cells naturally decreases with age.

9. Neurological Diseases

Stem cell therapy is a promising approach in the treatment of neurological diseases. In diseases such as Alzheimer's, Parkinson's disease, and spinal cord injuries, stem cells can support the regeneration of damaged neurons and reduce their functional impairment. From the perspective of regenerative medicine, stem cells enhance the body's ability to repair itself and support the healing of damaged tissues. Although the effectiveness of stem cells depends on the individual patient's condition, they offer new hope in the treatment of neurological diseases [25].

9.1. Parkinson's Disease

Stem cell therapy has shown quite positive results in the treatment of Parkinson's disease. The study found that stem cells can help improve motor function and replace dopamine-producing neurons in some patients. However, as the process is still in its development stage, its effectiveness will vary depending on the specific characteristics of each case. Thus, stem cell therapy is considered a promising method for the treatment of Parkinson's disease. However, further long-term observation and clinical studies are needed to determine its full effectiveness and safety [26].

9.2. Alzheimer's Disease

The main potential role of stem cells in the treatment of Alzheimer's disease is due to their neuroprotective and regenerative properties. Stem cells are thought to help reduce inflammation in the body, repair damaged neurons, and potentially reduce the accumulation of amyloid-beta protein. Researchers also note that exosomes derived from stem cells may stimulate nerve regeneration and improve memory mechanisms. In general, this therapy is still in the clinical research phase and requires further studies to fully confirm its effectiveness. As a result of the research, the following benefits are suggested:

Neuroprotective effects: Protect nerve tissue in the brain by reducing neuronal damage.

Reduction of inflammation: Slowing disease progression.

Potential for reducing amyloid-beta accumulation: Alleviating symptoms of the disease.

Improving memory and learning: Possible through signaling molecules derived from stem cells.

These possibilities of stem cell therapy make it a promising future approach to Alzheimer's disease [26].

10. Errors and Risks in Stem Cell Therapy

Because stem cells do not always function properly in the body, they can sometimes cause complications, including abnormal cell growth or tumor formation. If the body's immune system identifies the transplanted stem cells as foreign, it may immediately destroy them or cause harmful inflammatory reactions. Therefore, autologous stem cell therapy is considered safer than donor-based transplantation. Possible complications include:

Immune Rejection: Transplanted stem cells may be recognized as foreign and destroyed.

Incorrect Differentiation: Stem cells may transform into unintended cell types, damaging tissues.

Infection Risk: Extraction and transplantation procedures carry a risk of infection.

Additional Major Risks:

Tumor Formation (Oncogenic Risk): Poorly controlled differentiation may lead to malignant cell growth.

Immune Reactions: Transplanted cells may trigger strong immune responses.

Graft Failure: Transplanted cells may fail to engraft and produce new blood cells (especially in bone marrow transplantation).

Graft-versus-Host Disease (GvHD): Donor immune cells may attack the recipient's tissues.

Increased Infection Vulnerability: Immune suppression after transplantation increases.

Due to the risks mentioned, stem cells need to be used under highly professional clinical supervision [27].

11. Conclusion

The discovery and application of stem cells is considered one of the greatest advances in the history of medicine. They are widely used in many fields and continue to be widely used. One of the most notable aspects is their ability to slow down the aging process, and one of their greatest clinical importance is their role in the treatment of chronic and degenerative diseases. They are also of particular importance in transplantation therapies and regenerative medicine.

Stem cell therapy has shown significant results in the repair of heart, joint, liver, and nerve tissue injuries. They may have therapeutic benefits in wound healing, tissue regeneration, and diseases such as diabetic wounds and osteoarthritis.

Many studies also show potential fertility-enhancing effects in some cases. However, clinical trials are ongoing to determine safety with respect to tumorigenesis and other conditions. With the development of science and technology, it is expected that more and more obstacles to treatment will be removed. Stem cell approaches are currently being investigated for the treatment of neurological diseases, and their effectiveness is expected to increase in the future. According to some scientists, stem cells could allow for advances in human longevity, the regeneration of all tissues, and even adaptation to new environments, including life beyond Earth.

Author Contributions

Both authors contributed substantially to the study and approved the submitted version.

Conflict of Interest

The authors declare no conflicts of interest.

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Abbreviations

Embryonic Stem Cells (ESCs), Human Pluripotent Stem Cells (hPSCs), Induced Pluripotent Stem Cells (iPSCs), In Vitro Fertilization (IVF), Three-Dimensional (3D), Carbon Dioxide (CO_2), Mesenchymal Stem Cells (MSCs), Amyotrophic Lateral Sclerosis (ALS), Graft-versus-Host Disease (GvHD).

References

[1] Physiotherapists Tralee. (n.d.). *Stem cell treatment*. Accessed [October 25, 2025] https://www.physiotherapiststralee.ie/stem-cell-treatment/

[2] Becker, A. J., McCulloch, E. A., & Till, J. E. (1963). Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells. https://doi.org/10.1038/197452a0

[3] Ramalho-Santos, M., & Willenbring, H. (2007). On the origin of the term “stem cell”. *Cell stem cell*, *1*(1), 35-38. https://doi.org/10.1016/j.stem.2007.05.013

[4] Scholer, H. R. (2004). The potential of stem cells. An inventory. *Bundesgesundheitsblatt gesundheitsforschung gesundheitsschutz*, *47*(6), 565-577. https://doi.org/10.1007/s00103-004-0848-x

[5] Atala, A., & Lanza, R. (2012). Handbook of Stem Cells, Academic Press.

[6] Atta-ur-Rahman. (2017). *Frontiers in stem cell and regenerative medicine research* (Vol. 3). S. Anjum (Ed.). Sharjah: Bentham Science Publishers. https://doi.org/10.2174/97816810843501170401

[7] Slack, J. M. (2018). *The science of stem cells*. John Wiley & Sons. https://doi.org/10.1002/9781119235293

[8] Physiotherapists Tralee. (n.d.). *Stem cell treatment*. Accessed [October 25, 2025] https://www.physiotherapiststralee.ie/stem-cell-treatment/

[9] Siminovitch, L., McCulloch, E. A., & Till, J. E. (1963). The distribution of colony-forming cells among spleen colonies. https://doi.org/10.1002/jcp.1030620313

[10] Cong, Y. S., Wright, W. E., & Shay, J. W. (2002). Human telomerase and its regulation. *Microbiology and molecular biology reviews*, *66*(3), 407-425. https://doi.org/10.1128/mmbr.66.3.407-425.2002

[11] Shenghui, H. E., Nakada, D., & Morrison, S. J. (2009). Mechanisms of stem cell self-renewal. *Annual Review of cell and Developmental*, *25*, 377-406. https://doi.org/10.1146/annurev.cellbio.042308.113248

[12] Gugjoo, M. B. (2025). *Stem Cell-Based Regenerative Medicine in Canine Practice*. John Wiley & Sons. https://doi.org/10.1002/9781394253289

[13] Sekhar, L., & Bisht, N. (2006). Stem cell therapy. *Apollo Medicine*, *3*(3), 271-276. https://doi.org/10.1016/s0976-0016(11)60209-3

[14] Tuch, B. E. (2006). Stem cells: a clinical update. *Australian family physician*, *35*(9).

[15] Oliveira, P. H., Silva, C. L., & Cabral, J. M. (2014). Concise review: genomic instability in human stem cells: current status and future challenges. *Stem Cells*, *32*(11), 2824-2832. https://doi.org/10.1002/stem.1796

[16] Mitalipov, S., & Wolf, D. (2009). Totipotency, pluripotency and nuclear reprogramming. *Engineering of stem cells*, 185-199. https://doi.org/10.1007/10_2008_45

[17] Thomson, J. A., Itskovitz-Eldor, J., Shapiro, S. S., Waknitz, M. A., Swiergiel, J. J., Marshall, V. S., & Jones, J. M. (1998). Embryonic stem cell lines derived from human blastocysts. *science*, *282*(5391), 1145-1147. https://doi.org/10.1126/science.282.5391.1145

[18] Ulloa-Montoya, F., Verfaillie, C. M., & Hu, W. S. (2005). Culture systems for pluripotent stem cells. *Journal of bioscience and bioengineering*, *100*(1), 12-27. https://doi.org/10.1263/jbb.100.12

[19] Müller, A. M., Huppertz, S., & Henschler, R. (2016). Hematopoietic stem cells in regenerative medicine: astray or on the path?. *Transfusion Medicine and Hemotherapy*, *43*(4), 247-254. https://doi.org/10.1159/000447748

[20] Zhang, L., Mack, R., Breslin, P., & Zhang, J. (2020). Molecular and cellular mechanisms of aging in hematopoietic stem cells and their niches. *Journal of Hematology & Oncology*, *13*(1), 157. https://doi.org/10.1186/s13045-020-00994-z

[21] Aj, F. (1974). Precursors for fibroblasts in different populations of hematopoietic cells as detected by the in vitro colony assay method. *Exp hematol*, *2*, 83-92.

[22] Friedenstein, A. J., Gorskaja, U. F., & Kulagina, N. (1976). Fibroblast precursors in normal and irradiated mouse hematopoietic organs. *Experimental hematology*, *4*(5), 267-274.

[23] Kuroda, Y., Kitada, M., Wakao, S., Nishikawa, K., Tanimura, Y., Makinoshima, H., & Dezawa, M. (2010). Unique multipotent cells in adult human mesenchymal cell populations. *Proceedings of the National Academy of Sciences*, *107*(19), 8639-8643. https://doi.org/10.1073/pnas.0911647107

[24] Bone marrow transplant. (n.d.). In Encyclopædia Britannica. Accessed [October 27, 2025] https://www.britannica.com/science/bone-marrow-transplant

[25] Madan, A., Ashique, S., Arora, D., & Satapathy, M. K. (Eds.). (2025). *Stem Cell Therapeutics*. John Wiley & Sons. https://doi.org/10.1002/9781394313785

[26] Irfan, S., Etekochay, M. O., Atanasov, A. G., Prasad, V. P., Kandimalla, R., Mofatteh, M., & Emran, T. B. (2024). Human olfactory neurosphere-derived cells: a unified tool for neurological disease modelling and neurotherapeutic applications. *International Journal of Surgery*, *110*(10), 6321-6329. https://doi.org/10.1097/js9.0000000000001460

[27] Herberts, C. A., Kwa, M. S., & Hermsen, H. P. (2011). Risk factors in the development of stem cell therapy. *Journal of translational medicine*, *9*(1), 29. https://doi.org/10.1186/1479-5876-9-29