JJOAS
المجلة الأردنية للعلوم التطبيقية
Jordan Journal of Applied Science
Jordan Journal of Applied Science
Natural Science Series

Review

Stem cell therapy: A new and promising strategy for treating a variety of illnesses

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ARTICLE INFO

Article history:
Received 20 Mar 2021
Accepted 30 May 2021
Published 31 Dec 2021

DOI:

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Keywords:
Regenerative medicine.
Stem cells.
Stem cell technology.
Stem cell therapy.

ABSTRACT

Background: In both embryonic and adult tissues, stem cells are a subtype of cells that may self-renew and differentiate as necessary. Stem cells are categorized as ovarian stem cells, induced pluripotent stem cells (iPSC), spermatogonial stem cells (SSCs), adult stem cells (including mesenchymal stem cells, or MSC), and embryonic stem cells (ESC) based on where they come from. Stem cells can develop into many kinds of cells. The capacity to develop into a specific adult cell type and the capacity for constant self-renewal are the two traits that distinguish a stem cell. By repairing organ damage, stem cells in differentiated organs help to restore function. For patients with untreated illnesses and disorders, recent developments in stem cell technology provide a new avenue. Recently, stem cell-based therapy which includes multipotent mesenchymal stem cells (MSCs) and human pluripotent stem cells (hPSCs) has become a major force in regenerative medicine. With an emphasis on the application of stem cells in medical diseases as well as the advancements made in regenerative therapy methods for a number of disorders, this study describes the progress and obstacles being faced in the development of stem-cell-based therapies. The ethical and legal difficulties in converting autologous stem cell-based interventions into safe and efficient therapies are also highlighted, along with the limitations of these treatments and current difficulties in the field.

Conclusion: Cell-based therapy, particularly stem cells, offers new hope for patients with terminal illnesses when treatment focuses on managing the illness rather than curing it.

Introduction

The human body contains unspecialized cells called stem cells. They have the capacity to self-renew and can differentiate into any type of organism's cell. Both adult cells and embryos contain stem cells (1).

Stem cells can be broadly divided into two groups: "pluripotent" stem cells, which are induced pluripotent and embryonic stem cells, and "adult" stem cells, which are somatic or nonembryonic (2).

One of the major breakthroughs of the decade in stem cell research was the discovery of iPSCs in 2006. The idea that human somatic cells could be reprogrammed to become pluripotent embryonic stem cells excited the researchers and scientists (3).

This novel approach makes it possible to produce unique stem cells for every patient, which is essential to the customized medicine space. The fields of pharmacological screening, transplantation treatments, and disease modeling have all shown great potential using iPSCs. Mostly because they are made from the patient's own cells, which successfully lowers the risk of immunological rejection (4).

Stem cell therapy has emerged as one of the most promising and cutting-edge scientific study topics in recent years. The lack of transplantable organs has raised hopes that stem cells could be the solution to humanity's long-sought replacement of aging and disease-ravaged tissues. The advancement of therapeutic approaches has raised high hopes (5).

People suffering from a variety of illnesses now have hope thanks to the development of stem cell research, which has led to a wide range of clinical applications. Cardiovascular illness, neurological disorders, diabetes, and ophthalmology are among the specialties where these applications are most noteworthy (6).

Although the area of stem cell-based therapy has advanced significantly, the primary drawbacks of this therapeutic approach immunogenicity, limited cell supply, and ethical dilemma remain unresolved. MSCs have gained interest because of their potential as a source, high rate of multiplication, minimally invasive process, and lack of ethical concerns (7).

So, this study aimed to focus on the types of stem cells, describe the progress and obstacles being faced in the development of stem-cell-based therapies. The ethical and legal difficulties in converting autologous stem cell-based interventions into safe and efficient therapies are also highlighted.

Stem cells

Stem cells are a group of undifferentiated cells that have the capacity to divide into many cell and tissue types (potent), proliferate widely (self-renewal), and often originate from a single cell (clonal) (8).

Historical view

Drs. James A. Till and Ernest A. McCulloch of the University of Toronto in Canada described the first stem cells more than fifty years ago, in 1961. They discovered that mouse bone marrow-derived stem cells, known as pluripotent stem cells (PSCs), could differentiate into a range of cell types (9).

A few decades later, in 1996, Keith Campbell, Ian Wilmut, and associates at the University of Edinburgh's Roslin Institute cloned Dolly the sheep, proving the viability of somatic cell nuclear transfer (SCNT) (10).

Then, in the United States, James Thomson isolated the first human embryonic stem cells (hESCs) in 1998 (11).

John Gurdon (Gurdon Institute, Cambridge, UK) and Shinya Yamanaka (Kyoto University, Japan and Gladstone Institutes, USA) shared the 2012 Nobel Prize for Physiology or Medicine for discovering that mature cells may be reprogrammed into a pluripotent state (12).

The specialization process involves multiple steps. Because developmental potency decreases with each stage, a unipotent stem cell cannot differentiate into as many different types of cells as a pluripotent one (13).

One special quality of stem cells is their pluripotency; when given the right stimuli, a pluripotent cell can divide endlessly into daughter cells while still having the ability to develop into any type of human cell (14).

Stem cell classification according to potency

The degree of differentiation that stem cells can undergo into distinct cell types allows for their classification. totipotent, pluripotent, multipotent, and unipotent are the four primary categories (15).

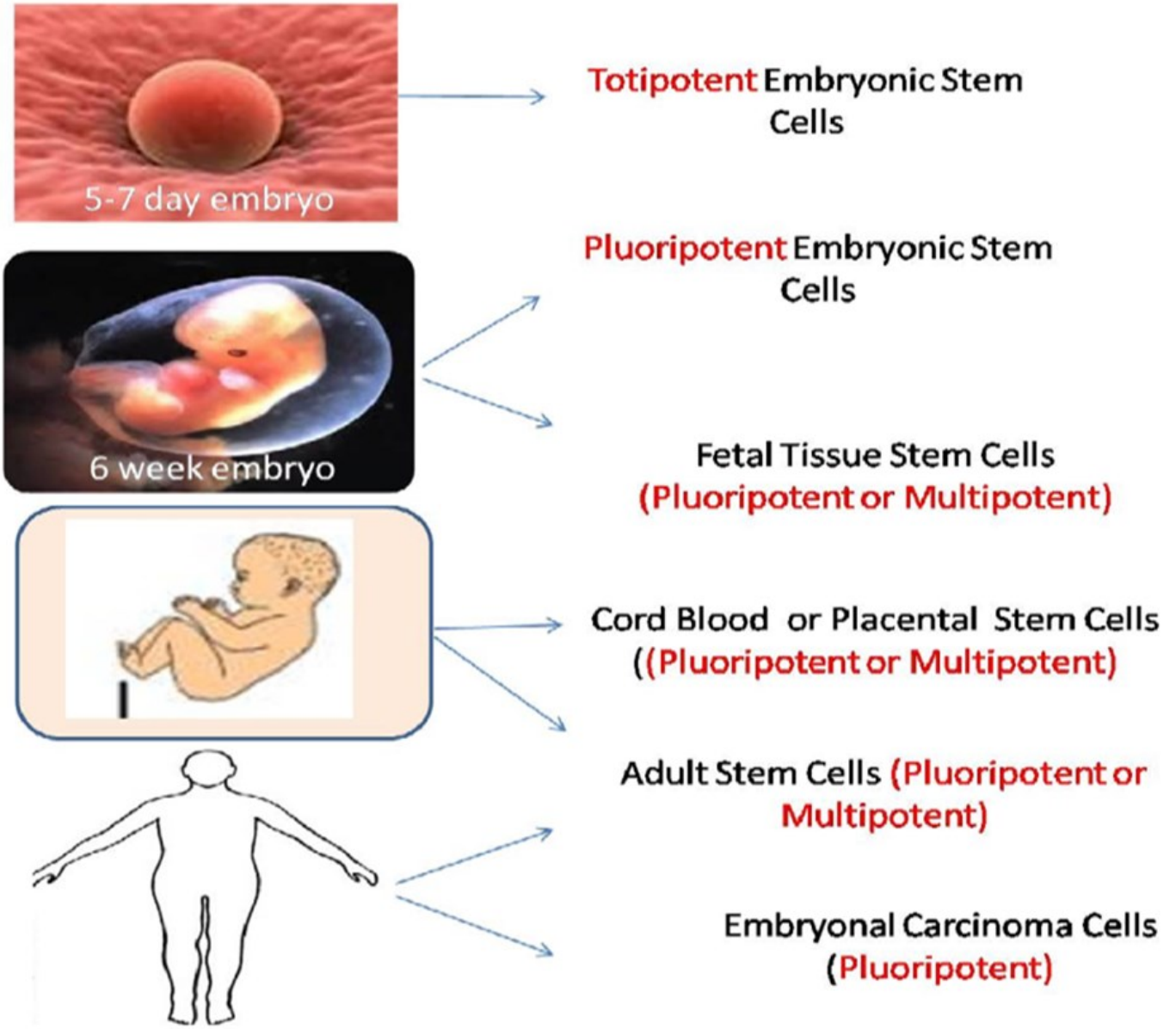


Figure 1. Stem cell classification according to potency (15).

Totipotent stem cells: It is possible for totipotent stem cells to divide and differentiate into cells that make up the entire organism. With the greatest capacity for differentiation, totipotency enables cells to develop into both embryonic and extra-embryonic structures. A zygote is a type of totipotent cell that develops when an egg is fertilized by a sperm. Later on, these cells may differentiate into a placenta or any one of the three germ layers. About four days later, the inner cell mass of the blastocyst develops pluripotency. This structure is where pluripotent cells originate (16).

Pluripotent stem cells (PSCs): The development of human embryonic stem cells (hESCs), which are pluripotent, has opened up new avenues for research in human toxicology, drug screening and development, the study of early embryonic development, the production of "spare parts," and the treatment of numerous degenerative diseases (17).

All germ layers' cells can be formed by pluripotent stem cells (PSCs), however extraembryonic tissues like the placenta cannot. One example is embryonic stem cells (ESCs). The inner cell mass of preimplantation embryos is the source of ESCs. Induced pluripotent stem cells (iPSCs), which are obtained from the epiblast layer of implanted embryos, provide an additional illustration. From fully pluripotent cells like ESCs and iPSCs to representatives with lesser potency: multi-, oligo-, or unipotent cells their pluripotency ranges (12).

Multipotent stem cells: Compared to PSCs, multipotent stem cells can specialize in distinct cells of particular cell lineages, but their range of differentiation is more restricted to a germinal layer [like mesenchymal stem cells (MSCs)] or simply a particular cell line (like HSCs), but they have less capacity for proliferation than the other two types. This category also frequently includes adult stem cells. These cells can develop into a closely related family of cells in the world (15).

Oligopotent stem cells: An oligopotent cell is created from a hematopoietic stem cell after differentiation. The cells of its lineage are then the only ones with differentiation capabilities. But since some multipotent cells can change into several kinds of cells, it's suggested that they be called pluripotent cells (18).

Unipotent stem cells: Research on unipotent stem cells has lagged behind that of totipotent and pluripotent stem cells, despite the latter two gaining popularity. When a stem cell can differentiate into cells with only one lineage, it is said to be unipotent. Among the examples of this sort of cell are muscle stem cells (15).

Unipotent stem cells have the limited capacity for differentiation and the unique ability to divide repeatedly. Their latter characteristic makes them a viable option for regenerative medicine therapy. These cells, such as dermatocytes, can only differentiate into one type of cell (20).

Stem cell classification according to their origins

Adult stem cells (ASCs), embryonic stem cells (ESCs), very small embryonic-like stem cells (VSELs), Induced pluripotent stem cells (iPSCs), Hematopoietic stem cells (HSCs) and nuclear transfer stem cells (NTSCs) are the fundamental types of stem cells (21).

Different sources can be used to generate or harvest each type of cell. The characteristics of each type of cell are explained as follows (12):

Adult stem cells.

Adult stem cells (ASCs) are a rare subset of cells that are predicted to be (i) quiescent, (ii) perform asymmetric cell divisions (ACD) to self-renew and produce tissue-committed "progenitors," and (iii) show "plasticity," which is the capacity to specialize into distinct lineages. In contrast to embryonic stem cells, which are "immortal," capable of differentiating into 200 different cell types, and identified by their place of origin (blastocyst's inner cell mass) (22).

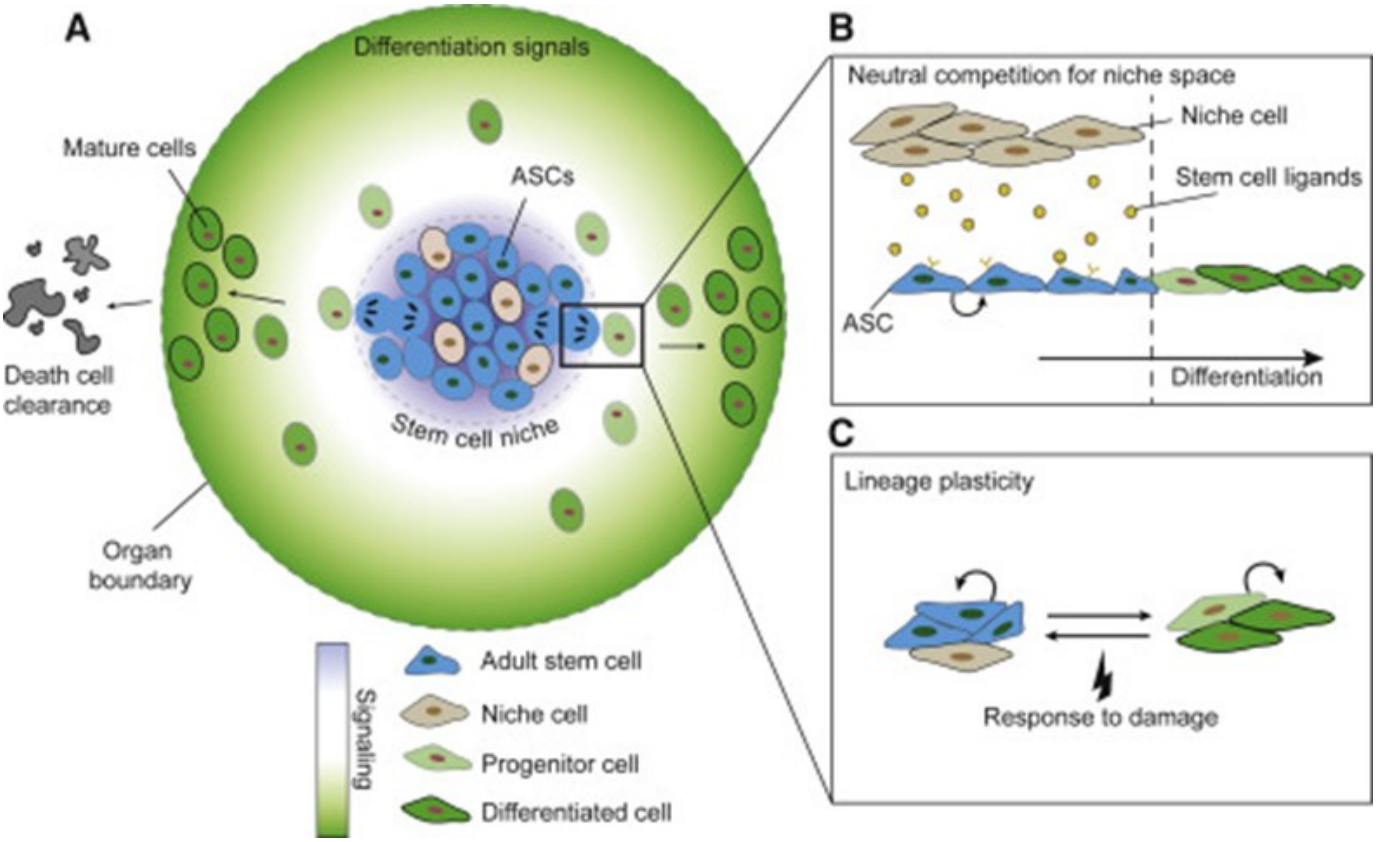


Figure 2. The Number of Stem Cells Depends on Niche Size (23).

When adult stem cells were originally identified, there was a lot of enthusiasm about their potential for translation, but there are still concerns regarding their potential for therapeutic use. Adult stem cells isolated from particular organs, such the heart, brain, or spinal cord, might provide a fresh approach to cell treatment. According to research on stem cells in adult organs, specific cues in their microenvironment are necessary for their survival, quiescence, and activity (12).

They frequently provide the impression of being able to identify damaged areas and dying cell types, only renewing the cells that are lost. Adult stem/progenitor cells that remain in tissue could be readily available sources for cell treatment (24).

These cells are capable of multilineage differentiation and strong self-renewal, which allows them to repair damaged tissues without facing immunological rejection. In contrast, as was previously mentioned, adult stem cells isolated from mature tissues may undergo reprogramming to become iPSCs. In situ stimulation of indigenous cells to proliferate and differentiate into particular cell types can also be accomplished with exogenous biological small molecules (22).

Embryonic Stem Cells

Human embryos are defined as the organism that is present in the uterus from the moment of implantation until the conclusion of the second month of pregnancy. However, embryonic stem cells (ESCs) describe a considerably more constrained time frame, as a result of the separation and culture of cells from the blastocyst, which develops about five days after conception (25).

The characteristics of cultured ESCs are as follows: they are immortal in culture and can be kept in the undifferentiated state for several hundred passages; they are pluripotent, meaning they can differentiate into cells from all three germ layers; and they retain a normal chromosomal makeup (27).

Well-developed molecular analysis of ESCs has revealed that they express a number of genes linked to pluripotency, including Oct-4, Rex-1, SOX-2, Nanog, LIN28, Thy-1, SSEA-3, and -4, as well as surface markers such CD9, CD24, and alkaline phosphatase. Their cultural immortality can be explained by the expression of high quantities of telomerase (28).

Very Small Embryonic-Like Stem Cells (VSELs)

Recently, Very Small Embryonic-Like Stem Cells (VSELs), a novel kind of pluripotent stem cell, have showed promise. These cells are called VSELs because of their primitive shape and gene expression profile. They are small, early development stem cells seen in adult tissues that exhibit pluripotency markers (12).

In terms of appearance, VSELs are tiny cells, which are comparable to the cells in the blastocyst's inner cell mass. These cells are somewhat smaller than red blood cells, measuring between 3 and 5 μm in mice and 5 to 7 μm in humans. Certain ESC markers, including SSEA, nuclear Oct-4A, Nanog, and Rex1, are expressed by VSELs according to their gene expression profile (29).

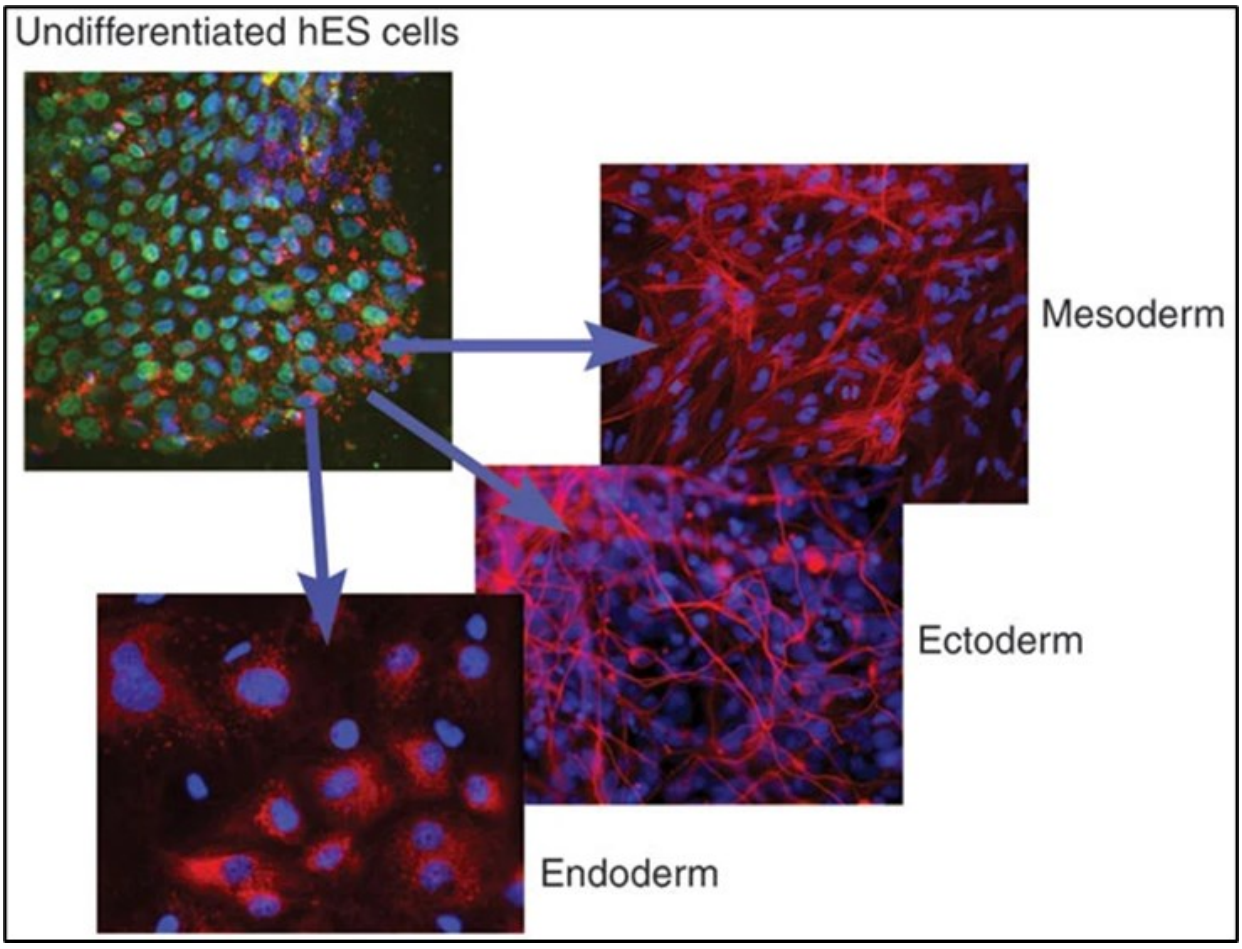


Figure 3. Immunocytochemical labeling shows an undifferentiated hES cell colony with positive immunoreactivity for Oct4 (green) and SSEA-4 (red). Cultures of hES cells differentiated in vitro show immunoreactivity for smooth muscle actin (mesoderm), beta-tubulin III (ectoderm) and alpha fetoprotein (endoderm) (26).

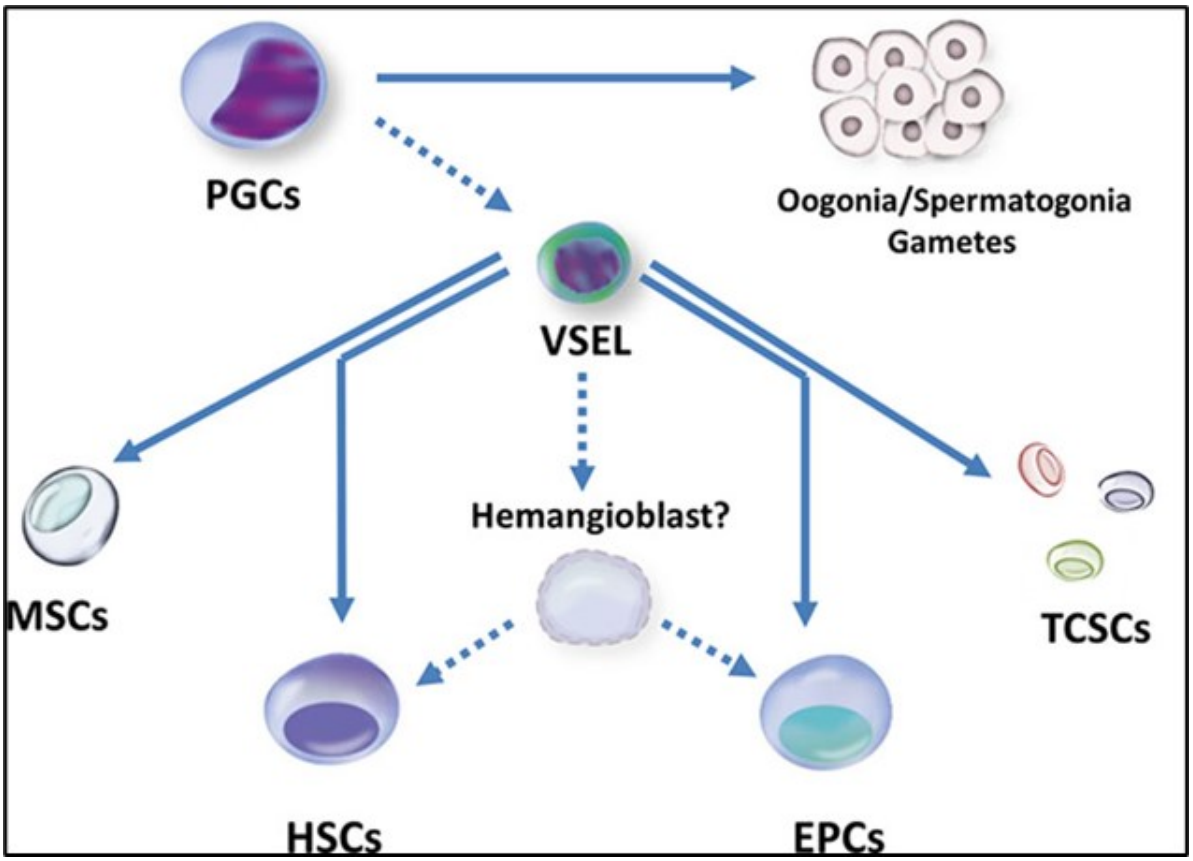


Figure 4. Proposed developmental interrelationship between primordial germ cells (PGCs), very small embryonic-like stem cells (VSELs), hemangioblasts, hematopoietic stem cells (HSCs), and endothelial progenitor cells (EPCs) (29).

VSELs began as primordial germ cells (PGCs) and underwent additional differentiation to become tissue-committed stem cells (TCSCs), mesenchymal stem cells (MSCs), and hemangioblasts, which are two subtypes of hematopoietic stem cells that include HSCs and endothelial progenitor cells (EPCs). VSELs may therefore have the potential benefit of being able to differentiate across germ layers in mature animals or human beings because they are pluripotent stem cells. In adulthood, these cells might serve as a substitute for monopotent tissue-committed stem cells (30).

Induced pluripotent stem cells (iPSCs)

Using mouse embryonic and adult fibroblast cultures, Yamanaka, S. and Takahashi, K. made a significant discovery in the early 2000s when they were able to produce new types of stem cells that resembled ESCs. These were known as induced pluripotent stem cells (iPSCs) (31).

Cell Type	iPSCs	ESCs
Source	Any somatic cell	Embryos
Advantages	• No ethical issues • Easy to obtain • Blood group compatibility • HLA histocompatibility • Disease modelling use • Drug/toxicity profiling • Efficient differentiation	• Established and characterized • Efficient differentiation • Disease modelling use
Disadvantages	• Reprogramming need • Oncogene activation risk • Early letality • High gene mutation rate • Genetic instability • Cost • MHC downregulation	• Blastocyst stage embryo destruction • Limited blastocyst days • Difficult obtention • High mutation rate • Genetic instability • Immunosuppresants • Tissue rejection • MHC downregulation

Figure 5. indicating the differences between iPSCs and ESCs, regarding their source(s), their advantages and disadvantages significant for their use as disease models and potential cell treatments (31).

Adding four transcription factors to the culture media: OCT4, SOX2, KLF4, and C-MYC, known as the Yamanaka factors, which help to induce and maintain the pluripotent state by integrating viral vectors, specifically retroviral and lentiviral transduction allows them to reprogram the gene expression of the fibroblasts' genome (32).

Induced pluripotent stem cells have been extensively employed in research on possible cell therapy, pharmacological screening for neuroprotective substances, and disease modeling (33).

Additionally, when iPSCs are combined with organoids and gene editing tools like CRISPR-Cas9, they become an extremely flexible tool for regenerative medicine and drug screening to assess substances that may be able to treat a variety of illnesses. As a result, clinical candidates are found and some are authorized for use (32).

Nuclear Transfer Stem Cells.

Transfer stem cells from the nucleus. NTSCs can currently be produced via the somatic cell nuclear transfer (SCNT) technology, which was first identified in 1996. Starting with an enucleated oocyte (i.e., cytoplasmic donor or egg donor with nucleus removed), SCNT first implants a donor nucleus (i.e., nucleus donor) from another fully developed somatic cell (e.g. fibroblast) (34).

Reprogrammed Stem Cells.

Yamanaka and colleagues created iPSCs for the first time in 2006, but reprogramming methods have advanced a lot since then. In vitro and in vivo direct reprogramming techniques that use tiny compounds or chemicals, RNA signal changes, and lineage-restricted transcription factors to create particular tissue-lineages are particularly noteworthy in this regard (12).

Bypassing the iPSCs stage, these direct methods produce more accurate cells, including induced neural progenitor cells (iNPCs), which are nearer the target cell lineage, including neural cells and later motor neurons. Therefore, any manual laboratory approach that reprograms the genetic signals of the primary cells can be used to create reprogrammed stem cells (RSCs); however, the SCNT technique is not one of them (35).

Hematopoietic stem cells

HSCs are multipotent cells that undergo hematopoiesis to produce blood cells. Throughout an animal's or human's life, these bone marrow-resident cells renew all adult hematopoietic lineages (36). Furthermore, these cells may survive freezing for many years and can replace damaged or absent hematopoietic and immune system components (15).

Individual HSCs can generate all blood lineages: in other words, they are multipotent. While daughter cells continue to divide, they migrate down the hierarchy and become progressively lineage restricted. This occurs through a well-orchestrated series of discrete steps and eventually yields mature blood cells of the various types. In sum, HSC identity is hardwired. The homeostatic renewal hierarchy is rigidly designed. Cells flow unidirectionally through the system, from the HSC through the various progenitor stages to the terminally differentiated cell types, after which death ensues (23).

Stem cell culture

For differentiation and development, stem cells need a combination of nutrients and growth hormones. Every day, the medium should be switched. Cell culture is the process of cultivating cells in a lab (21).

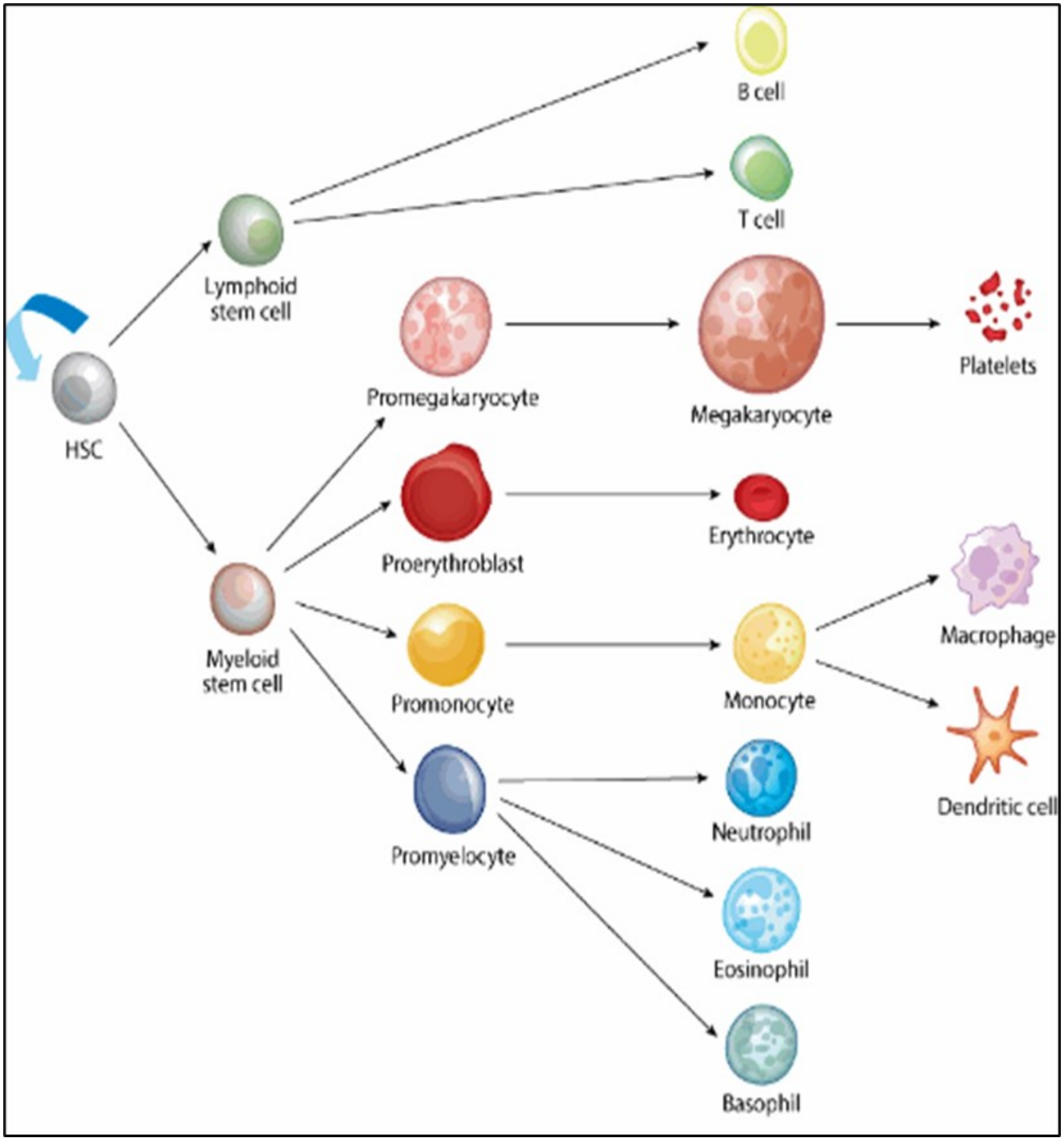


Figure 6. The classical hematopoietic stem cell (HSC) hierarchy. The HSC is rare and quiescent, while the flow through the hierarchy is strictly unidirectional, away from the HSC. The HSC is the only cell that can act as a stem cell (23).

The process of creating human embryonic stem cells (hESCs) involves putting cells from a preimplantation stage embryo onto a plastic laboratory culture dish that is filled with culture medium, a nutritional broth. The cells proliferate and disperse across the dish's surface (37).

StemPro, synthetic serum substitute (SSS), knockout serum replacement (KOSR), or serum (such as fetal calf serum FCS) can be used as the initial culture medium. Only eight necessary components are present in the most basic culture media: DMEM/F12 medium, selenium, NaHCO3, l-ascorbic acid, transferrin, insulin, TGFβ1, and FGF2 (38).

Stem cell lines

A stem cell line is a group of healthy, proliferating, undifferentiated cells that have been permitted to divide and proliferate in a controlled culture (20).

A single parent group of stem cells produces a family of continuously dividing cells also known as a stem cell line. They are derived from either human or animal tissues and have a lengthy half-life in vitro (15).

Using light, the technique known as flow cytometry counts and profiles the cells in a combination of different fluids. It makes it possible for scientists to quickly and precisely gather data from mixtures of different fluids containing living cells. A tiny channel is used to pass cells one at a time. Sensors pick up light that the cells emit or reflect when exposed to light. Data analysis, compilation, and integration into a complete sample picture constitute the last step (1).

Applications of stem cells

Because of their ability to develop into a wide variety of cell types, stem cells have greatly increased the expectations of medical professionals, researchers, patients, and the general public (39).

MSCs from humans are plastic-adherent cells that can develop

into ectoderm and endoderm-derived cells.3 to 5. Furthermore, they are capable of changing into distinct mesenchymal lineages and leaving behind their undifferentiated or unspecialized stages (40).
Therefore, in both physiological and experimental settings, they can restore bone, cartilage, and fat as well as develop into endothelium, muscle, or neuronal cells. MSCs were initially extracted from mononuclear cells originating from bone marrow (BM), although evidence suggests they are found in nearly all human tissues (41).
Because MSCs are in charge of wound healing, tissue repair, growth, and cell replacement brought on by physiological or pathological factors, they can be used therapeutically to treat conditions affecting the central nervous system, such as spinal cord injuries (42).
The discovery that multipotent adult stem cells could be reprogrammed to become pluripotent by scientists Shinya Yamanaka and Kazutoshi Takahashi in 2006 marked a sea change in stem cell therapy. This procedure prevented the life of the fetus from being in jeopardy. Mouse fibroblasts may become pluripotent if they are transduced by a retrovirus containing four transcription factors (Oct-3/4, Sox2, KLF4, and c-Myc) that are primarily expressed in embryonic stem cells (1).
Researchers studying stem cells are working on a variety of projects, including as curing hereditary illnesses and creating novel human tissues and biomaterials produced from stem cells for application in regenerative medicine and pharmaceutical genomics (43).
Findings from finished and ongoing clinical trials show that stem cell-based therapy has enormous therapeutic promise for the treatment of hereditary, autoimmune, and degenerative diseases (12).
Regenerative medicine primarily encompasses two distinct cell-based therapeutic approaches. In the first method, damaged cells are replaced within a tissue to restore its integrity and functionality. This process, known as "cell therapy," involves merely injecting a cell suspension into the bloodstream or into the injured tissue. The second strategy is more intricate and is referred to as "tissue engineering." In order to replace missing tissue or even entire organs, cells are mixed with a three-dimensional matrix to create a tissue-like structure (44).

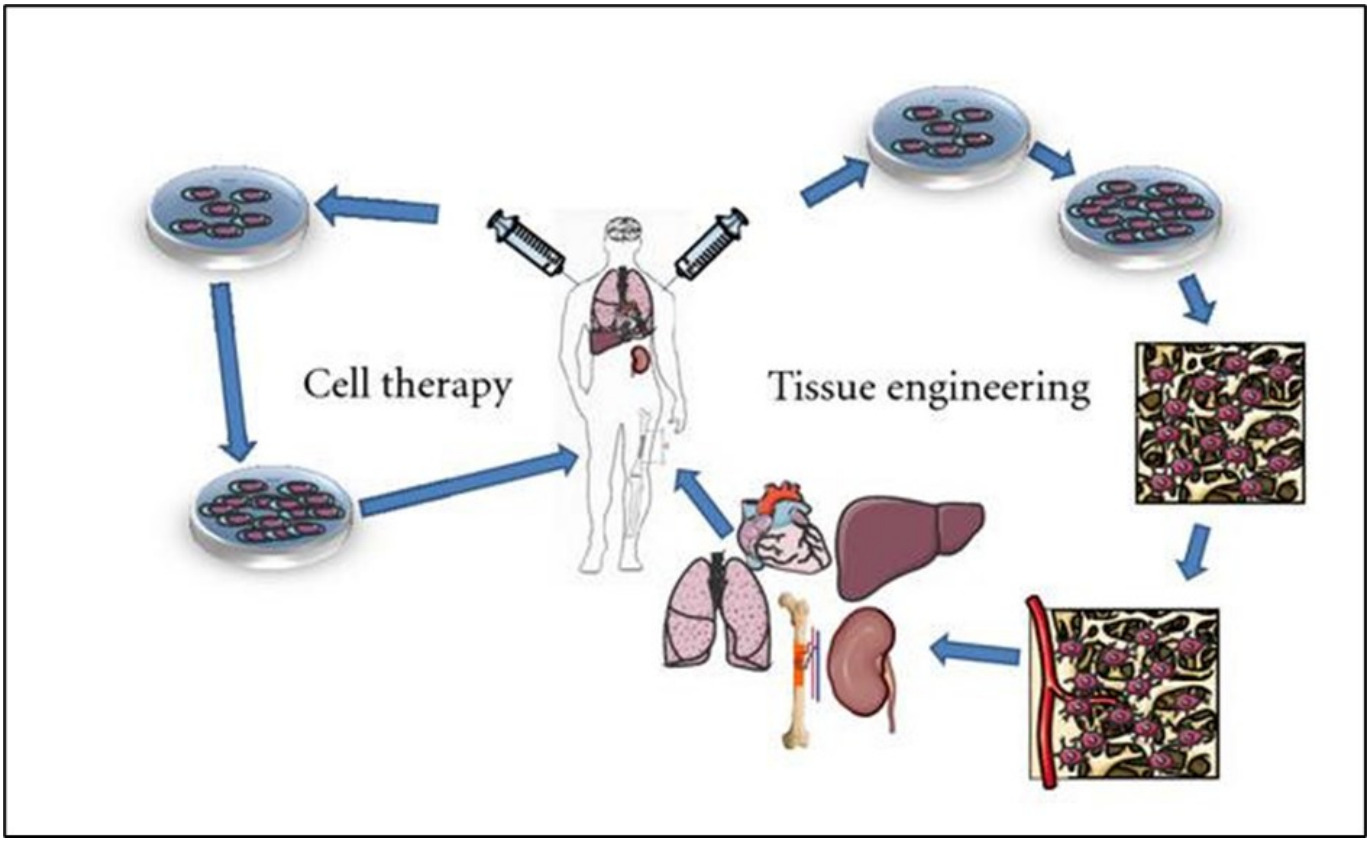


Figure 7. the two methods used in regenerative medicine to apply stem cells. In autologous transplantation, stem cells are extracted from the patient; in allogenous transplantation, they are extracted from other donors. To replace lost cells, the cells are grown in vitro and either administered directly to the patient (cell therapy) or planted into three-dimensional scaffolds (tissue engineering) and developed into the desired cell type. The created artificial tissue construct is then placed into the tissue defect of the patient (44).

Hematopoietic stem cell transplantation is among the most effective forms of "cell therapy." For decades, this process has been used to treat severe hematological disorders. Hematopoietic stem cells are infused into the recipient's bloodstream in order to transplant bone marrow. It's interesting that they use a process known as "homing" to locate the bone marrow. It was discovered that chemokines are essential for hematopoietic stem cell homing (45).

Phenotypic pluripotency assays: Successful stem cell therapy depends on the ability to identify undifferentiated cells. With a large nucleolus and a high nucleus to cytoplasm ratio, among other traits, stem cells seem to have a unique shape. Unlike developing colonies, which look as loosely distributed cells with bumpy borders, cells appear as flat with distinct borders (46).

Inadequate cell division or differentiation is the root cause of many severe medical disorders, including cancer and birth abnormalities. Stem cell therapies are now being developed to treat a variety of conditions, including diabetes type 1, retinal and macular degeneration, spinal cord injury, heart failure, and tendon ruptures. Understanding stem cell physiology can be improved with the aid of stem cell research. This could lead to new approaches to treating diseases that are presently incurable (1).

The ability of iPS cells to differentiate and proliferate indefinitely makes them appealing for both current and future scientific fields. They are a vital source of human tissue for medical examinations and can be kept in a tissue bank. Conventional differentiated tissue cells kept in a lab setting have the drawback of losing their propagation characteristics over time. iPSCs don't experience this (47).

The range of possible stem cell-based therapies has increased recently as a result of advancements in stem cell research, even though stem cell-based treatments have been established as the clinical standard of care for certain conditions, such as hematopoietic stem cell transplants for leukemia and epithelial stem cell-based treatments for burns and corneal disorders (15).

It is well known that mesenchymal stem cells are abundant in the umbilical cord. Because it is cryopreserved as soon as it is born, its stem cells can be successfully preserved and utilized in treatments to stop a patient's future life-threatening illnesses (48).

There are several stem cells therapies available, however aside

from bone marrow transplantation, the majority are either expensive or in the experimental stage (49).

Stem cells from adults and embryos are expected to be used in the near future to treat a wide range of conditions, including cancer, Type 1 diabetes, Parkinson's disease, Huntington's disease, celiac disease, heart failure, neurological problems, muscle damage, and many more diseases. They contend that additional study is required to comprehend stem cell behavior following transplantation and the processes of stem cell interaction before stem cell therapies may be used in a clinical setting (50).

Despite their modest success, regular infusions of beta cells produced from stem cells would be a more effective treatment. It has been demonstrated that iPSCs can develop into beta cells in large enough numbers to react to variations in blood sugar levels (51).

Neurons and glial cells in the brain or spinal cord of the Central Nervous System (CNS) are lost in human neurological illnesses such Alzheimer's disease (AD), Parkinson's disease, stroke, or spinal cord injury (52).

The use of stem cell technologies to study and treat various illnesses has grown in popularity. Stem cells have been effectively used to create a variety of neuronal and glial cell types, which have occasionally improved certain dysfunctions in both clinically treated people and animal models of neurological illnesses (50).

Acute kidney injury (AKI) can be improved by using BM-MSC and microvesicles. Furthermore, HUCMSC-EXO has demonstrated both in vitro and in vivo therapeutic benefits on cisplatin-induced nephrotoxicity. Cisplatin is an anticancer medication that causes nephrotoxicity by causing renal tubular epithelial cells to undergo apoptosis due to oxidative stress. However, blood urea nitrogen (BUN), proximal kidney tubule necrosis, apoptosis, and creatinine (Cr) levels have all decreased after HUCMSC-EXO treatment (53).

In an animal model, muscle-derived MSCs (M-MSCs) were able to develop into osteoblasts and repair a major femoral lesion after being transfected with the bone morphogenetic protein-4 gene, demonstrating the wide range of clinical uses for M-MSCs. These cells have also been applied to craniofacial regeneration in a similar way (54).

The direct implantation of M-MSCs with fibrin glue into osteochondral lesions in an animal model led to the defect site's continuous healing after 24 weeks. When these cells develop, they produce extracellular matrix that is rich in proteoglycans and type II collagen (55).

Skin regeneration following severe skin damage, such as that brought on by burns, chronic ulcers, and deep wounds, as well as anti -aging treatment and repigmentation in cases of vitiligo, alopaecia, and melanoma, are significant uses for the skin derived MSCs (S-MSCs). S-MSCs are also being researched for potential clinical uses in bladder restoration, alopecia, spinal cord injuries, and the regeneration of the hematopoietic lineage following radiation therapy (56).

In mouse models of sciatic and tibial nerve transections and crush injuries, undifferentiated hair follicle stem cells have also been employed; following cell injection, the mice show better functional results (57).

The progress and obstacles being faced in the development of stem-cell-based therapies.

Theoretically, MSCs can be extracted from nearly any tissue in the human body, but in practice, this is limited by the invasiveness and difficulty of the procurement procedure as well as different donor characteristics. The practitioner must take into account both the potential negative effects of harvesting the donor's cells and the challenge of obtaining the samples in order to choose a suitable cell source (57).

For instance, BM-MSCs might cause pain, hemorrhage, or infection, which makes it more difficult to harvest MSCs from this source than from peripheral blood, surgical leftovers such AT, or tissues acquired at birth .

Expectations have grown beyond our existing knowledge and laws governing the use of stem cell treatment due to the vast range of opportunities it has created. In order to fulfill these expectations, the Food and Drug Administration (FDA) in the United States has promoted additional research to evaluate the advantages and disadvantages of stem cell therapy and provide evidence-based treatment strategies (40).

Only stem cell therapies derived from BM aspirate concentrate have received FDA approval to yet (57).

Although hematopoietic reconstitution using MSCs obtained from BM or peripheral blood is a well-established, safe, and successful treatment, nothing is known about the safety and effectiveness of MSCs produced from other sources. These sources might occasionally be used with scant clinical support (58).

The ability of MSCs to repair damage, the high expense of clinical trials that require significant industrial sponsors, and the belief that stem cell therapies are safe, particularly when sourced from an autologous source, are some of the justifications offered for these practices (59).

Modern clinicians should be aware of the fundamentals of regenerative medicine, the range of clinical alternatives available to them, and how these therapies may influence medical choices. They must, however, also shield patients against popularized pseudomedical procedures that are marketed as stem cell therapy. Because transplantable stem cell production proceeds at a somewhat slow pace, the majority of therapeutic alternatives for stem cell therapy concentrate on chronic illnesses. Prior to a therapeutic response being observed, such techniques often need the acquisition, isolation, growth, differentiation, and implantation of a sufficient number of cells (58).

For safe and suitable stem cell transplantation, the Food and Drug Administration and the European Medicines Agency have established Good Manufacturing Practice (GMP) criteria. Animal-derived products were formerly necessary for stem cell transplantation methods (60).

There have been attempts to employ BM-MSCs in a therapeutic setting to treat cardiomyocyte loss, ease heart failure, and prevent end-stage heart failure. A meta-analysis of ten large-scale randomised phase two trials using BM-derived cells revealed no benefits following an acute myocardial infarction, despite the encouraging results of clinical trials in both human and animal models (57, 61).

The ethical and legal difficulties in converting autologous stem cell-based interventions into safe and efficient therapies are also highlighted.

The vast range of opportunities that stem cell therapy has created has led to expectations that beyond our existing knowledge and laws governing their application. The Food and Drug Administration (FDA) in the United States has pushed for additional research to evaluate the advantages and disadvantages of stem cell therapy and provide evidence-based treatment strategies in order to achieve these expectations (62).

Some of the justifications for these practices include the belief that stem cell therapies are safe, particularly when sourced from an autologous source; the ability of MSCs to repair damage; and the requirement for large industrial sponsors due to the extremely high cost of clinical studies (59).

The foundation of regenerative medicine, the therapeutic alternatives available to them, and the potential for these therapies to influence medical decisions should all be understood by the modern practitioner. They must, however, also shield patients from pseudomedical procedures that have gained widespread acceptance as stem cell therapy (40).

Due to the comparatively sluggish rate of transplantable stem cell production, the majority of clinical alternatives for stem cell therapy concentrate on chronic illnesses. Generally speaking, before a therapeutic response is observed, such techniques necessitate the acquisition, isolation, growth, differentiation, and implantation of a significant number of cells (49).

There are exceptions to long-standing safety restrictions for regenerative medicine goods in several nations. In Japan, for instance, these medications are only needed to achieve lower standards for therapeutic efficacy in order to be sold, based on early data (63).

However, regardless of cell source or clinical use, clinical trials should be conducted to guarantee the safe and efficient use of therapies employing MSCs. Furthermore, particular legislation ought to be put into place to further regulate the use of these cells (58).

Finally, It may be feasible to mimic the precise function of native tissues in the future by differentiating MSCs that are identical to the organs that require replacement, once the aforementioned difficulties have been overcome. Additionally, in vivo differentiation could result in standardized stem cell treatments for a range of illnesses.

Conclusion

Cell-based therapy, particularly stem cells, offers new hope for patients with terminal illnesses when treatment focuses on managing the illness rather than curing it.

Disclosure

None to be disclosed.

Conflict of interest

None.

Data sharing plans

Data will be available upon request.

Funding information

The authors guarantee that no funding was granted for this work.

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