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The Potential Of Stem Cell Therapy

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Abstract

The study of stem cell therapy has led to the development of a very advanced, promising, and effective method for conducting scientific research. This success has ushered in a new era of treatment through various paths of dividing patterns. After the regeneration of stem cells, different lab procedures are used to cultivate distinct cell types. Quality control and teratoma development assays are among the methods used to evaluate the growth kinetic characteristics of the stem cells. To determine the best natural-type environmental conditions for a certain differentiation, various culture mediums are tested. Extracellular vesicle-based therapies and graphene scaffolds, which have enormous therapeutic potential due to their adaptability, are some of the structures used. This review focuses on the discovery of many stem cells and their potential for therapeutic use in modern medicine. The wide range of stem cell functions creates a very effective technique that offers an alternative for disorders that cannot be cured. The objective of the review is to draw attention to the stem cell treatment system among researchers.

Keywords: *Embryonic stem cells, Stem cell therapy, Totipotent, Undifferentiated cells*

1. Introduction

Extremely undifferentiated cells exist in the embryonic, fetal, adult, and mature stages of life. These are called stem cells (Davenport et al., 2022). They split to become differentiated cells, or G0 stage, which is the building block of life (Kuntawala and McCann, 2021; Shih et al., 2007). Tissue-specific stem cells found in organs are present from birth and can repair damaged organ tissues. (Chowdhury, 2023; Kolios et al., 2013). Their ability to do arithmetical division, differentiate into functional cells of a live creature, and self-renewal is astounding (Neofytou, 2023; Miotti et al., 2021). Specialization occurs in several synchronous phases (Pagliari et al., 2014). A stem cell with unipotency is differentiated into a single kind of cell since developmental potency continues to decline with each phase (Zakrzewski et al., 2019). According to Rajabzadeb et al. (2019), the main characteristics of stem cells are their ability to self-renew, create clones, and have high potency. The

characteristics of various stem cells may vary. For instance, adult tissue stem cells have a limited capacity for self-renewal, would not proliferate widely, and could only differentiate into cells specific to a related tissue, whereas embryonic stem cells (ESCs) come from the embryonic stage of the blastocyst and have a greater capacity for self-renewal nature and high potency power (Hall et al., 2009).

The zygote is the starting point for organism development, which continues through blastocysts with ESCs that are differentiated into the 3 germ layers of ectoderm, mesoderm, and endoderm (Zoldan et al., 2011). These three distinct germ layers divide in various ways to produce various organs (Poh et al., 2014). Diverse progenitor cell types that divide to produce organ formation do not terminally/permanently differentiate aside from maintaining the capacity to function as tissue stem cells and can be found in abundance in the bursa of babricus in bone marrow, long bones, blood cells, muscle part, lobules of the liver, brain, fat storing adipose tissue, dermal layer of skin, and the lower region of the gastrointestinal tract (Stangler et al. These cells may be arrested in the G0 stage within tissue but would proliferate or enter the G1 stage under conditional circumstances of tissues repair and injury (Mu et al., 2011). The stem cells in tissue may be known by the name of progenitor cells while they divide to finally differentiated and specialized cells present in tissue or organ (Byder et al., 2006). In the lobule of the liver, the long bone's bone marrow, the lung, and the intestinal part of the gut, stem cells frequently proliferate or divide to form supplement cells during normal tissue turnover or injury, whereas in other organs like the pancreas, heart, or nervous system, they divide to replace damaged cells after injury (Odonoghue et al., 2004; Rana et al., 2017; Otto et al.).

With the first attempts at bone marrow transplantation in animals in the 1950s, the new scientific era of medicine began with trials on stem cell therapy and organ regeneration procedures (Martin et al., 2008). These ground-breaking accomplishments paved the way for human bone marrow transplantation, a procedure that is now often used to treat many blood-related illnesses (Chinen et al., 2010). The existence of stem cells that are used to restore mature tissue was revealed thanks to this ground-breaking treatment strategy (Pellegrini et al., 2009). Regenerative medicine is currently a leading area of study, not only to find treatment systems but also to comprehend basic biology and the pathophysiology of diseases (Synder et al., 2018). Even though some moral or ethical questions have come up in stem cell research, recent advances in stem cell isolation and development have helped the scientific community recognize and mediate specific cell types for tissue regeneration in a variety of disorders like Parkinson's disease related to the brain, Alzheimer's disease related to memory, or diseases related to pacemakers in the heart, muscles, lung, liver, and other organs (Zocchi et al., 2019).

2. Classification of Stem Cells

2.1 Classification according to ability to differentiate

According to their ability to differentiate, stem cells can be divided primarily into five groups: totipotent, pluripotent, multipotent, oligopotent, and unipotent (Kastenberg et al., 2008).

2.1.1 Totipotent To create an entire creature, totipotent stem cells first divide by geometric mitosis and then further through the arithmetic mean of mitosis (Bogdan et al., 2014). They are capable of the greatest degree of differentiation and direct dividing cells to produce both extra-embryonic and embryonic traits. According to Ishiuhi et al. (2013), the human zygote or embryo up to the eighth cell stage is the most notable example of totipotency. Monozygotic twins are examples of totipotency. The inner cell mass of the blastocyst reaches pluripotency after approximately 4 days or after 16 cell stages.

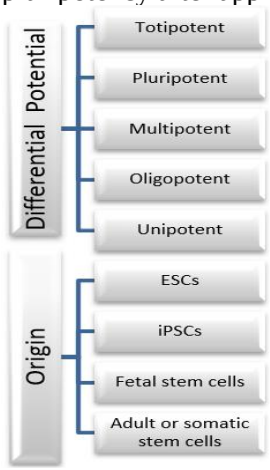

Fig 1: Types of Stem Cell

2.1.2 Pluripotent stem cells (PSCs) can differentiate into a wide range of cell types in all germ layers, however they cannot produce additional embryonic structures, such as the placenta (Liu et al., 2020). Embryonic stem cells (ESCs) are capable of producing entire organs. Pre-implantation embryos' inner cell mass is a reliable source of ESCs (Hall, 2008). On media containing serum and leukemia inhibitory protein/factor or media free from serum supplemented with extra 2 inhibitory pharmaceuticals ("2i"), the MEK inhibitor PD03259010 & GSK-3 inhibitor CHIR99021, the self-renewal property does not let the cells from clumping or aggregating. Pluripotent stem cells (iPSCs) can be found in abundance in the epiblast layers of implanted embryos (Dakhore et al., 2018). Beyond pluripotency, the cells can develop into multi-, oligo-, or unipotent cells with low potency. Teratoma development assays are methods used to access their broad spectrum and mode of action (Zakrzewski et al., 2019). Scientists have now discovered a mechanism to intentionally create iPSCs from somatic cells, and these cells divide in a manner reminiscent of PSCs. Their methods of division, cultivation, and use usher in a new age for regenerative medicine. **Beta cells** in the pancreas were once made from pluripotent stem cells, or pancreatic stem cells. In patients with hyperglycemic situations, the proliferation of these stem cells would present a unique cell source for drug research and cell or tissue transplantation/histocompatibility treatment (Jiang et al., 2014). Beta cell apoptosis occurs every 40 to 50 days. Pancreatic duct stem cells divide and undergo differentiation to become brand-new islet cells.

2.1.3 Multipotent stem cells According to Yoon et al. (2011), multipotent stem cells have a high level of specialization in producing distinct cells from specific cell lineages while showing less differentiation than PSCs. Three different types of blood cells can be produced by hematopoietic stem cells (Giarratana et al., 2005). **Neural Stem Cells** Adult mammalian brains include neural stem cells that are multipotent and capable of self-replication. These cells are growing in certain molecular settings. They can demonstrate a possible function in brain cellular treatment (Temple, 2001). **Gastrointestinal stem cells** The gastrointestinal/gut tract contains stem cells, which are found in a "niche" in the area of the crypts and salivary glands that make up the intestinal wall. There is considerable debate on the mechanisms underlying the diffusion of this transformed clone throughout the mucosa of the gastrointestinal system (Britan et al., 2002). **Hepatic stem cells** The liver has the unique ability to regenerate, using different pathways depending on the nature and severity of the injury or wound. Adult liver cells have the capacity to divide in order to regenerate parenchymal tissue and repair damaged or non-functional tissue. The oval cell ductular reaction mechanism, also known as chronic hepatic injury, is a potential or active stem cell compartment located in the intrahepatic biliary tree (Forbes et al., 2002).

2.1.4 Oligopotent Cells A cell becomes an oligopotent cell after differentiating or being stopped at the G0 stage. The cells in its lineage are then the only cells that can differentiate. However, certain multipotent cells possess the plasticity to differentiate into other cell types. According to Majo et al. (2008), oligopotent stem cells have a wide range of cell types they can develop into. Myeloid stem cells can undergo mitosis and divide to produce WBCs but not RBCs.

2.1.5 Unipotent cells have the most limited differentiation capacities. Unipotent stem cells can divide to produce cells of the same lineage, such as dermatocytes. The flexibility property in regenerative medicine opens a novel treatment avenue (de Kreter et al., 2007). **Epidermal stem cells** According to Blanpain et al. (2006), the epidermal layer is a rapidly rejuvenating tissue that contains three types of keratinocytes with varying degrees of differentiation potential: the first type is epidermis stem cells, the second type is transiently amplified cells (TA cells), and the third type is terminally/finally differentiated cells. The epidermis contains stem cells that are capable of unrestricted self-renewal. While TA cells, newly generated cells from the epidermal stem cells, finally go differentiation stage after 3-5 divisions, they have the potential to maintain homeostatic environment and the power of cellular regeneration of injured skin, capability of wound healing, and power of neoplasm development (Janes et al., 2002). TA cells travel from the basal layer to the suprabasal layers to the tissue surface after dividing, and wherever they exist, they periodically drop as squames (Watt et al., 2006).

2.2 Classification of Stem Cells Using Differentiation Potential and point of origin of differentiation

One of the two primary features of stem cells, the capacity to differentiate, differs amongst stem cells according to their place of origin and lineage. Stem cells are categorized based on their potential and point of origin of differentiation. Based on where they come from, stem cells can be divided into four broad categories: ESCs, fetal and adult stem cells, and iPSCs (Muller et al., 2008). Adult stem cells are oligopotent or unipotent, whereas ESCs and iPSCs are typically pluripotent.

2.2.1 Embryonic stem cells (ESCs), which are derived from the pre-implantation embryonic blastocyst stage, have the property of being pluripotent. ESCs can divide through mathematical mitosis, then differentiate into three major germ layers, while half of the cells can also remain undifferentiated for a long time in culture conditions (Bishop et al., 2002). In the blastocyst stage, there are two layers of cells: the inner cell mass, which divides by mathematically mitosis to produce the embryo, and the trophoblasts, which are the outer cell mass and which also divide by mathematically mitosis to produce the placenta. To propagate ESC lines, cells from the inner cell layer are moved to a culture medium under highly precise microenvironments. The transcription factors Nanog and Oct4 are used to confirm the existence of ESCs (Andrews, 2002). These transcription factors maintain the stem cells' undifferentiated status, which gives them the ability to self-renew. ESCs that preserved their undifferentiated status and had virtually no chromosomal or genetic defects during arithmetic mitosis were propagated as an ESC line. These cells could be cryo-preserved, then thawed for continued growth in culture conditions for research and therapeutic systems. Maintaining culture conditions to keep ESCs in an undifferentiated state is quite difficult. Leukemia Inhibitory Factor (LIF), an anti-differentiation cytokine, is employed to cultivate embryonic fibroblast cells (Martello et al., 2014).

2.2.2 Adult Stem Cells Adult/mature tissue is used to isolate adult stem cells. MSCs made from amnion epithelial cells of human placental tissue are one example. According to Young et al. (2004), these cells demonstrate considerable anti-inflammatory and tissue repair system enhancement abilities. Even though these cells have the ability to develop into tissue under in vitro settings from a variety of germ cell layers, their only limitation is that they only have a limited capability for differentiation. The advantages of self-regeneration using adult stem cells do not raise questions about graft rejection. The three germ layers, placenta, and developing embryo are the best sources of adult stem cells.

2.2.3 Tissue-Resident Stem Cells Tissue-resident stem cells, which regenerate specific-tissue, terminally differentiated function G0 arrested cells, are crucial for tissue renewal and injury repair in adult stages (Muehlberg et al., 2009). These cells are thought to form during ontogenesis and stay dormant until local cues trigger their proliferation, differentiation, or migration. A "niche of stem cells" is where tissue-resident stem cells live. The stem cell niche is a particular micro level intracellular environment that controls the cell's capacity for self-renewal and differentiation. The activity of stem cells is strongly impacted by extrinsic signals, and as a result, the niche or microenvironment is important for stem cell homeostasis and tissue repair. The majority of tissue-resident stem cells are dormant under normal circumstances, but they become active in response to specific signals after healing and damage (Raveh et al., 2013). The niche environment affects the tissue-resident stem cells' dormancy. Dormancy is a crucial component of cell size maintenance because it prevents cells from completing any other tasks besides producing tissue-specific cells during tissue healing procedures. The molecular environment that causes stem cells to display a self-renewal property, proliferate, and differentiate must be studied, as well as tissue-specific signals. Additionally, the sorts of cell division a stem cell experiences affects the kinds of cells it produces. In order to replenish damaged cells after injury, a stem cell must divide symmetrically in order to produce identical daughter cells. In order to maintain the function of organ repair, the stem cell homeostatic environment must be balanced because unchecked stem cell proliferation can lead to stem cell hyperplasia or the phenomenon of carcinogenesis (Pinilla et al., 2009). When a stem cell produces two distinct daughter cells, one identical and the other differentiated, this is known as asymmetric division. This procedure keeps a population of stem cells alive while allowing for organ regeneration and repair.

Table: Types of Stem Cells

Type of Stem Cell	Source	Characteristics	Differentiation Potential
Embryonic Stem Cells (ESCs)	Embryos	Pluripotent (can become almost any cell type)	High
Induced Pluripotent Stem Cells (iPSCs)	Somatic cells (e.g., skin cells) reprogrammed in the lab	Pluripotent (similar to ESCs)	High
Adult or Somatic Stem Cells	Tissues (e.g., bone marrow, adipose tissue)	Multipotent (can differentiate into a limited range of cell types)	Moderate
Hematopoietic Stem Cells (HSCs)	Bone marrow, blood	Multipotent (can give rise to various blood cell types)	Moderate
Mesenchymal Stem Cells (MSCs)	Bone marrow, adipose tissue, other tissues	Multipotent (can differentiate into bone, cartilage, fat cells, etc.)	Moderate

Neural Stem Cells (NSCs)	Nervous tissue	Multipotent (can differentiate into various neural cell types)	Moderate
Epithelial Stem Cells	Skin, intestine, other epithelial tissues	Multipotent (can generate specific cell types within the tissue)	Moderate
Olfactory Ensheathing Cells	Olfactory nerve tissue	Multipotent (can differentiate into nerve-related cells)	Moderate
Totipotent Stem Cells	Early-stage embryonic cells	Can give rise to all cell types, including embryonic and extra-embryonic tissues	Very High (can form an entire organism

3. Clinical Relevance

3.1 Diabetes mellitus and stem cells Stem cells have an extraordinary capacity to regenerate damaged or dead cells, tissues, and organs. As a viable alternative to transplantation, stem cell treatment has provided Type 1 diabetic patients with access to pancreatic glucose-responsive beta cells (Hussain et al., 2004). Based on their surroundings, mesenchymal stem cells (MSCs) will either divide and differentiate or function. It is expected that MSCs will particularly differentiate into pancreatic cells with exocrine and endocrine secretion and function properties when put into the pancreas organ in vivo. As a result, the pancreatic region can be repaired by the transplantation of MSCs made from bone marrow-derived stem cells by imparting paracrine effects and other cellular differentiation (Soejitno et al., 2011).

3.2 Parkinson's disease and stem cell therapy Parkinson's disease (PD) is a neurological condition that affects people all over the world because so few nigrostriatal dopamine (DA) neurons are present. MSCs have a remarkable capacity for differentiation into neurons with a tyrosine hydroxylase-positive enzymatic system, and they can improve mice's motor neurons. Animals with human MSC transplants demonstrated improved motor nerve function (Lindvall, 2003).

3.3 Heart illness and stem cells Cardiologists are hoping for a novel method of treating their patients who have cardiac diseases. Transferring stem and progenitor cells into the heart helps improve the wounded heart's tissue perfusion and contractile function. According to Janssens et al. (2010), stem cells have the potential to progress the treatment of individuals with acute myocardial infarction, coronary artery problems, and chronic heart failure.

3.4 Autoimmune disorders When we have an autoimmune disorder, our immune system assaults our own healthy tissues. MSCs are utilized to treat autoimmune disorders. Patients with severe autoimmune diseases typically require autologous or allogeneic hematopoietic stem cell transplantation (HSCT) (Davidson et al., 2001). Patients with severe autoimmune diseases do not respond to conventional treatment.

3.5 Cirrhosis and liver failure are caused by poor dietary habits, as well as a number of other chronic hepatic ailments. Because of their capacity for regeneration and immunomodulation, MSCs have a great capacity to treat liver problems. MSCs have been revealed to have the potential to modulate the immune system by causing the growth of regulatory T cells or by generating inhibitory cytokines. According to Kallis et al. (2007), MSC therapy is effective at controlling the immune response of the body in cases of tissue damage, organ transplantation, and liver autoimmune problems.

3.6 Kidney disease It has been demonstrated experimentally that the lifespan of embryonic renal SCs with nephrogenic potential is short. There is an interesting requirement for stem cells to continuously replenish the space left by lost cells because at least 6000 cells from various nephron segments are excreted through urine every hour. Chronic damage to an adult kidney may result in tissue regeneration and numerous structural alterations. The quest for resident renal stem/progenitor cells (RSPCs) has been substantially aided by these. MSCs can go to damaged kidney tissue or cells and create a variety of cytokines that have anti-inflammatory effects as well as chemokines that can change the path of an injury. Through endocrine or paracrine pathways, MSCs activate the body's mending system, which leads to tissue and cellular replacement and immune response repair (Hopkins et al., 2009).

3.7 Stem cells are used in skeletal muscle healing. Congenital muscular illnesses, such as Duchenne muscular dystrophy, can have their pace of progression slowed by using stem cells after autologous intramuscular transplantation. When stem/progenitor cells engraft into skeletal muscle, they divide in a special way that adds new myonuclei and corrects the genes whose expression is altered in myopathies (Gharaibeh et al., 2008).

3.8 Stem Cell therapy utilizing mesenchymal stem cells to restore sperm motility while controlling sperm glucose metabolism. A urological disorder called testicular torsion may result in sterility due to ischemia damage. Surgery (orchiopexy) is used to restore spermatogenesis. After testicular torsion-detorsion, mesenchymal stem cells (MSCs) were injected locally to reestablish the spermatogenesis process without differentiating into sperm (Hsiao et al., 2019).

3.9 Stem cell therapy is used to treat premature ovaries. This novel method may lead to the return of sexual hormone levels, activation of follicular cells, angiogenesis of the ovaries, and restoration of ovarian function. Paracrine actions, which can release a number of deceptive factors for the stimulation of ovarian angiogenesis, favor the function of stem cells (Sheikhansari et al., 2018).

3.10 Patients with lung disorders such emphysema, pulmonary associated hypertension, and advanced chronic obstructive pulmonary disease are treated by giving them mesenchymal stem cells. The United States and Canada have recently approved clinical trials to investigate a variety of cell therapy techniques for lung disorders (Porzionato et al., 2019).

3.11 Traumatic brain injury (TBI) is the main cause of morbidity and mortality in humans and can cause severe neurological impairment. The current research has demonstrated that different exogenous stem cells can migrate to dead or injured brain tissue, where they are then involved in the repair of dead brain by further dividing and differentiating to replace damaged cells, as well as releasing various growth factors and anti-inflammatory proteins, significantly improving neurologically related function (Maegele et al., 2008). It elaborates the significant sound signal pathways of stem cells in the part of the inner ear by inducing the division and differentiation of multipotent endogenous and connective tissue derived exogenous stem cells, the implantation procedure and regulation of connective tissue derived exogenous stem cells after implanted into the inner ear (Egger et al., 2020). Stem cell therapy uses intranasal stem cell treatment to help mice regain their sense of smell. A mouse's olfactory lobe can regain its sense of smell after receiving stem cell delivery (Kurtenbach et al., 2019).

Table 2: Clinical Significance of Stem Cells

Type of Stem Cell	Clinical Relevance
Embryonic Stem Cells (ESCs)	Potential for regenerative medicine, tissue replacement therapy. Ethical concerns and immune rejection issues must be addressed.
Induced Pluripotent Stem Cells (iPSCs)	Disease modeling, drug testing, and potential for personalized regenerative medicine. Addresses ethical concerns associated with ESCs.
Adult or Somatic Stem Cells	Used in bone marrow transplants for treating blood-related disorders. Potential for tissue repair and regeneration in various organs.
Hematopoietic Stem Cells (HSCs)	Commonly used in bone marrow transplants for treating leukemia and other blood disorders.
Mesenchymal Stem Cells (MSCs)	Investigated for their potential in treating conditions such as osteoarthritis, autoimmune diseases, and tissue damage.
Neural Stem Cells (NSCs)	Studied for potential use in treating neurological disorders and injuries.
Epithelial Stem Cells	Relevant in tissue repair and regeneration, particularly in skin and intestinal tissues.
Olfactory Ensheathing Cells	Investigated for their potential in spinal cord injury treatments.
Totipotent Stem Cells	Not currently used in clinical applications due to ethical concerns and complexities.

1. Future Implications of Stem Cell Therapy

The potential of stem cells is enormous and could revolutionize medicine in several ways. Stem cells, especially induced pluripotent stem cells (iPSCs), have the potential to repair or replace damaged tissues and organs. This could bring about a new era of treatment for various conditions such as heart disease, diabetes, neurodegenerative disorders, and spinal cord injuries. Stem cells also allow researchers to study different

diseases in controlled environments, which can lead to a deeper understanding of diseases and more effective drug development. With patient-specific iPSCs, personalized medicine becomes possible, allowing tailored therapies, disease modeling, and drug testing. Stem cells may also be used in tissue engineering to create functional tissues and organs for transplantation, which could address the shortage of donor organs. Stem cells are also vital in the development of immunotherapies, cancer stem cell therapies, and potential treatments for neurological disorders. However, ethical considerations, safety concerns, and the need for regulatory frameworks remain crucial aspects to navigate in the ongoing journey of stem cell research. The future may witness breakthroughs in anti-aging therapies, the creation of artificial organs, and innovative solutions for extending healthy lifespans, making stem cells a driving force in shaping the future of healthcare and medical interventions.

2. Conclusion

Stem cells possess extraordinary characteristics, such as the ability to multiply for extended periods and generate fully functional and specialized cells that contribute to the development of living organisms. The study of organogenesis patterns and the human body's inherent ability to regenerate using stem cells is a possibility. These cells have the potential to assist in the creation of a model for the investigation of the progression of pathogenesis and may aid researchers in comprehending the pathophysiology of various diseases. They provide a novel approach to creating diverse biological models that can be utilized to evaluate new pharmacological treatments. However, the most significant potential of these stem cells is their ability to replace damaged cells, tissues, and even organs. The current availability of several research findings, preclinical studies, and clinical outcomes has resulted in the development of new medications with therapeutic potential. There is a plethora of research and development taking place today, providing us with optimism about the future of regenerative medicine.

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