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Review on Stem Cell Therapy for the Treatment of Various Diseases and Conditions

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ABSTRACT

This comprehensive review paper examines the diverse landscape of stem cell therapy, focusing on its potential for tissue regeneration and repair through cell differentiation. It covers various stem cell types, from embryonic to adult stem cells, and discusses advanced techniques for their therapeutic use. The paper presents case studies and trial results demonstrating progress in medical applications. Ethical concerns and controversies are addressed, alongside widespread medical implementations from neurology to cardiovascular care. The review also forecasts substantial growth in the global stem cell therapy market, spotlighting key players and recent advancements. Overall, it offers a detailed glimpse into the transformative abilities of stem cell therapy in healthcare.

INTRODUCTION:

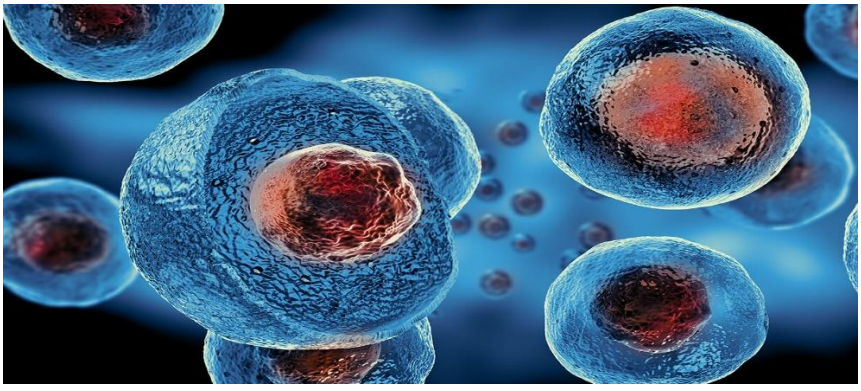
In recent years, stem cell therapy has emerged as an immensely promising and advanced field of scientific research, captivating the attention of researchers and medical professionals alike. The development of innovative treatment methods involving stem cells has sparked a wave of great expectations within the scientific community and among patients seeking ground-breaking therapies for various medical conditions.

This comprehensive review paper aims to delve into the fascinating world of stem cells, shedding light on their diverse types and remarkable potential as therapeutic agents. Stem cells possess the unique ability to differentiate into specialized cell types, offering the tantalizing prospect of regenerating and repairing damaged tissues or organs within the human body.

One of the key areas of focus in this review is the discovery of different types of stem cells, ranging from embryonic stem cells derived from early-stage embryos to adult stem cells found in various tissues, such as bone marrow and adipose tissue. Each type of stem cell holds distinctive characteristics and applications, fuelling the exploration of a wide array of potential treatment approaches.

Furthermore, the review will examine the cutting-edge techniques and methodologies employed in harnessing the therapeutic potential of stem cells. Scientists are continually refining their understanding of stem cell behavior and optimizing the protocols for their isolation, expansion, and manipulation to enhance their therapeutic effectiveness.

Throughout the paper, preclinical and clinical trial studies will be discussed to illustrate the progress made in translating stem cell research into tangible medical interventions. These insights will provide a glimpse into the current state of stem cell therapy and offer a glimpse of its future prospects. [1]



For years, scientists have been fascinated by the remarkable regenerative power of stem cells. This has led to a lot of curiosity and research into how they could be used for medical treatments. Stem cells can turn into different types of cells, which has the potential to completely transform the field of medicine.

Researchers worldwide have dedicated countless hours to unlocking the secrets of stem cells, seeking to harness their power to treat a myriad of illnesses that were once considered difficult, if not impossible, to manage effectively.

These ground-breaking achievements have opened new avenues of hope for patients suffering from various diseases, offering them a chance at improved quality of life and even potential cures.

In the field of regenerative medicine, stem cell therapies are proving very effective in diagnosing and treating degenerative diseases like Parkinson's, Alzheimer's, and spinal cord injuries. These conditions, once considered untreatable, are now being addressed with innovative stem cell treatments, offering hope to patients for a better future.

Moreover, stem cells have demonstrated their capacity to assist in the retreat and regeneration abilities of damaged tissues and organs. This holds particular significance for conditions that involve tissue damage or organ failure, like heart disease, diabetes, and liver cirrhosis. By harnessing the regenerative capabilities of stem cells, researchers have witnessed promising results in preclinical and clinical studies, providing a glimmer of hope for patients who once faced limited treatment options.

As the research and development of stem cell therapies continue to advance, there is a growing sense of excitement within the scientific community and among patients. The potential to revolutionize modern medicine and provide effective treatments for a wide range of diseases is within reach, and the positive impact on global healthcare could be profound. [2]

Stem cells are remarkable cells that have the special capability to change into different types of specialized cells through a process called differentiation. This means they can become muscle cells, brain cells, and many other types of cells in the human body.

Furthermore, stem cells can renew themselves through cell division, even if they've been dormant for a while. The area of stem cell research has received significant attention and

become crucial in the medical world due to its potential to transform regenerative medicine profoundly. By studying stem cells, scientists aim to unravel the intricate process of how an organism develops from a single cell into a complex living being.

This deep understanding could prove invaluable in identifying new treatments and therapies for various diseases and conditions. Amongst the primary goals of stem cell research is to explore the potential of using healthy cells to replace malfunctioning or damaged cells in both human and animal bodies.

The concept of tissue and organ regeneration holds tremendous potential for addressing a diverse range of medical conditions that affect various body systems and organs. From neurological disorders to cardiovascular diseases, stem cells offer a hopeful prospect for developing more effective and targeted treatments. However, while stem cell research and investigation bring the hope of medical advancements, it also faces significant ethical concerns.

The controversy arises mainly from the sources of stem cells and the techniques used to derive them. For instance, embryonic stem cells are exceedingly multipurpose and hold immense potential for medical or curative applications.

Still, their use involves the destruction of human embryos, raising ethical questions and debates surrounding the beginning of life and the rights of the unborn. On the other hand, adult stem cells, found in various tissues and organs of the body, offer a more ethical approach as they can be obtained without harming embryos.

Nevertheless, their differentiation capabilities are more limited compared to embryonic stem cells, posing challenges in certain regenerative medicine applications. Despite these ethical dilemmas, the exploration of stem cells continues with a strong focus on finding alternative sources and innovative techniques to harness their regenerative potential responsibly. [3]

Stem cells possess an extraordinary potency to metamorphose into various cell class while also retaining the competence to self-replicate and maintain the essential quality of their parent cells, a property alluded to as potency.

As a result, extensive research has been conducted to comprehend human evolution and organogenesis, leading to significant advances in stem cell-establish therapies and the field of regenerative medicine.

One area where these advancements have shown great assurance is in the medical care of ophthalmic circumstances, some of which are major causes of astigmatism worldwide. Stem cell therapies have demonstrated positive outcomes in addressing these conditions.

Additionally, encouraging results have been achieved in the treatment of oral and maxillofacial defects, showcasing the potential of stem cells to aid in tissue regeneration. Stem-cell-established therapies also hold great potential in treating chronic medical conditions like diabetes and cardiomyopathy.

The uncommon property of stem cells to migrate toward cancer cells makes them extraordinary vectors for transporting bioactive agents or aiming both primary and metastatic cancer cells, presenting a promising approach to cancer treatment. However, despite these promising therapeutic strategies, they are not without limitations.

One concern is the failure to completely eradicate tumors, leading to tumor relapse in some cases. Furthermore, stem cells dividend certain characteristics with cancer stem cells, raising concerns about potentially increasing the risk of cancer events when using stem cell therapies.

Ethical reasons related changes to the fatal origin of some stem cells also pose significant obstacles to the widespread put into effect of such therapies. Additionally, the cost of stem cell-based treatments can be prohibitive for many patients, limiting accessibility to these potentially life-changing therapies.

Overall, while stem cell research and therapies offer exciting possibilities for medical advancements and disease treatment, addressing these limitations and ethical considerations will be crucial in realizing the full capacities of on the basis of stem cell regenerative medicine in the future. [4]

HISTORY:

In recent years, stem cell therapy has become a promising field of scientific research with the potential to revolutionize medical treatments. This comprehensive review paper explores the diverse types of stem cells and their potential for regenerating damaged tissues and organs.

Table 1: Key events regarding stem cell therapy. [6-9]

Timeline	Key-events
1882	Early proposals of the stem cell concept by various researchers.
1888	The term "stem cell" was coined by German scientists Boveri & Haecker.
1902	Alexander M. Maximow identified hematopoiesis, the formation of blood components.
1958	The first successful stem cell therapy, a bone marrow transplant, was performed.
1963	McCulloch and Till demonstrated the existence of stem cells.
1969	The first American bone marrow transplant was performed.
1981	Embryonic stem cells were first isolated and cultured by British biologists.
1998	American biologist James Thomson isolated human embryonic stem cells.
2006	Induced pluripotent stem cells (iPS cells) were created in Japan.
2008	Successful cartilage regeneration in the human knee using adult mesenchymal stem cells.
2009	Stem cell transplant showed promise in curing HIV.
2009	President Obama reversed restrictions on stem cell research.
2010	First clinical trial of human embryonic-derived stem cells for spinal cord injury.
2012	Gurdon and Yamanaka won the Nobel Prize for reprogramming mature cells into pluripotent stem cells.
2015	UK NHS set up a stem cell factory for diabetes treatment.
2016	Surgeon involved in the first trachea transplant from the patient's own stem cells was sacked for misconduct.
2016	Stem cells showed substantial recovery in stroke patients.
2017	Personalized stem cell treatment effective for macular degeneration.
2017	Growing skin, bone marrow, and blood vessels using plant scaffolds with stem cells demonstrated.
2017	Gene therapy halted the progression of adrenoleukodystrophy in clinical trials.
2018	Significant differences were found in gene expression between body's stem cells and lab-cultivated stem cells.
2018	Stem cell-based treatment showed promise for age-related macular degeneration.
2018	Skin cells are reprogrammed into immune cells to fight cancer.
2019	Gene therapy promising for infants born with SCID-X1.

STEM CELL THERAPY:

Definitions

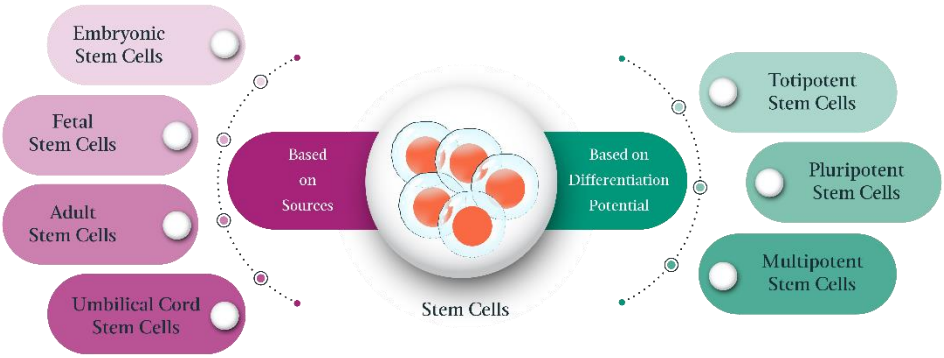
Stem cells are cells that are able to renew themselves through mitotic cell division and embryonic stem cells (ESCs) originate from the inner cell mass of a blastocyst at the early stages of embryo development. These cells are called totipotent because they can potentially transform into any cell type found in the human body.

Human ESCs offer promising applications in medical fields like tissue repair and regenerative medicine due to their ability to transform into various cell types. [11]

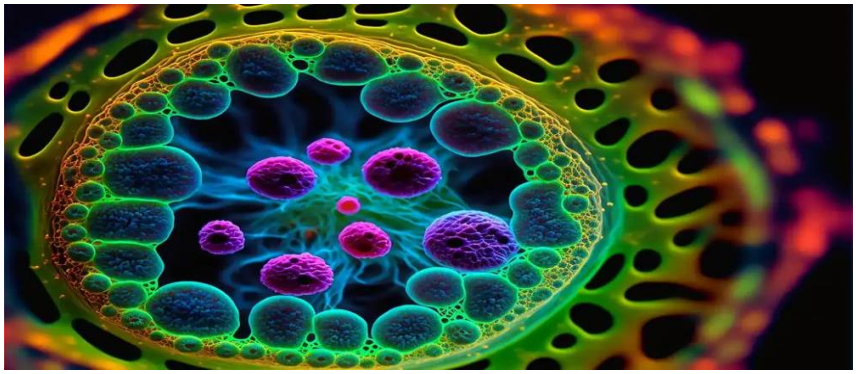
CLASSIFICATION:

Stem cells can be categorized into four main types based on their origin: embryonic stem cells, fetal stem cells, umbilical cord stem cells, and adult stem cells. These can further be divided into subtypes. Some researchers propose that adult and fetal stem cells might have evolved from embryonic stem cells.

The limited number of stem cells found in adult organs could be remnants of the original embryonic stem cells that either stopped differentiating into developing organs or reside in specific niches in the organs. These cells may be activated for tissue repair during injuries. [10]



1. Embryonic Stem Cells [ESC'S]



Following fertilization by sperm, an embryo begins to take shape. About 3-5 days later, it reaches the blastocyst stage, housing stem cells with the capability to become any cell type within the body. In the early stages of pregnancy, this blastocyst phase lasts for approximately 5 days before it implants in the uterus, and during this time, stem cells start their journey toward becoming different cell types. [12]

The study showed that embryonic stem cells [ECS's] can turn into functional neurons, suggesting they could be valuable for studying nervous system development and developing treatments for neurological disorders. [11]

2. Adult Stem Cells [ASC's]

Adult stem cells are undifferentiated cells present in various tissues throughout the body, and they can be categorized into different cell types. These cells have a crucial role in preserving the specific tissues where they are located and possess the potential to be harnessed for tissue repair and regenerative medical purposes.

Somatic stem cells, commonly referred to as adult stem cells, have been extensively studied in scientific research due to their potential applications in treating various diseases such as Diabetes, Parkinson's Disease, spinal cord injury, chronic inflammation, and potentially aiding in slowing the aging process.

It's crucial to highlight that the utilization of these somatic\adult remains a vibrant field of ongoing research. Further investigations are imperative to comprehensively grasp the extent of these cells' capabilities and to formulate reliable and efficient therapeutic approaches employing adult stem cells. [11]

3. Fatal Stem Cells [FSC's]

A recently identified category of stem cells falls under the label of Foetal stem cells (FSC). These are a novel kind of stem cells sourced from the fetus or structures originating from fetal tissue. Importantly, they do not give rise to teratomas and have different subtypes depending on their origin, such as amniotic fluid, umbilical cord, Wharton's jelly, amniotic membrane, and placenta. Fatal stem cells are easily accessible and exhibit a high rate of proliferation, making them well-suited for regenerative medicine. They can be seen as an intermediate stage between embryonic stem cells and adult stem cells (SSCs).[13]

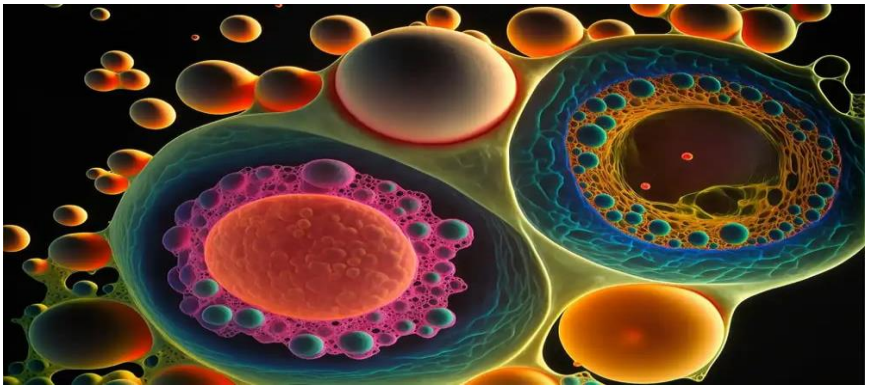
Haematopoietic Stem Cells

Ernest McCulloch and James Till, working as a cellular biologists and a biophysicist at the University of Toronto in the early 1960s, made a significant discovery. They found hematopoietic stem cells (HSCs) and conducted experiments on mice to demonstrate their role in forming blood cells.

Later on, it was revealed that HSCs possess the remarkable ability to self-renew, which is one of the defining characteristics of stem cells. [5]

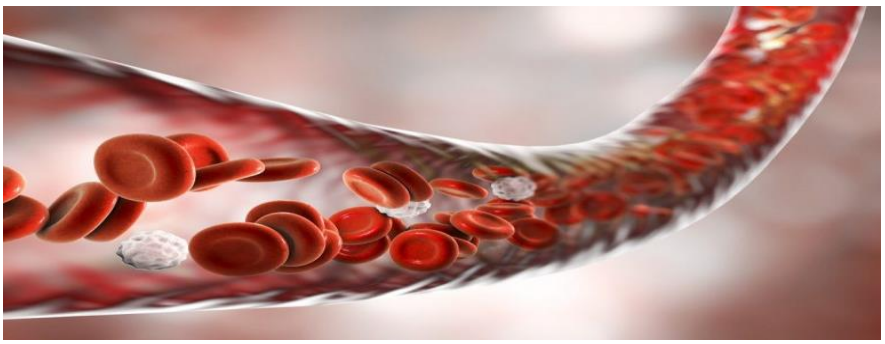
4. Mesenchymal stem cells (bone marrow stroma)

Mesenchymal stem cells (MSCs) are versatile cells with self-renewal and multi-lineage potential. They can be extracted from various tissues, like umbilical cords, bone marrow, and adipose tissue, due to their practicality. New sources, like menstrual blood and endometrium, have also been discovered. Understanding MSC differentiation, mobilization, and homing is a challenge. Their potential clinical applications are promising, especially in disease treatment, and future research should focus on their role in differentiation, transplantation, and immune response. [14]



Emerging findings have brought to light the existence of an uncommon pluripotent cell within the cultures of mesenchymal stem cells (MSCs). This extraordinary cell possesses a unique capability: not only can it give rise to tissues of the mesodermal lineage, but it also demonstrates the remarkable power to generate endodermal tissues, expanding its potential impact across multiple tissue types. [10]

5. Umbilical Cord Stem Cells



Umbilical Cord Blood (UCB) stem cells have emerged as a dependable option for treating various blood diseases when collected and frozen right after birth. This approach offers a straightforward and secure method of preserving genetic material for potential future therapies, serving as a viable substitute for bone marrow. With its abundant availability, uncomplicated collection process, and minimal ethical concerns, human umbilical cord blood presents a valuable alternative to other sources of stem cells. This article aims to examine existing literature on human umbilical cord blood (HUCB) and evaluate its potential applicability in disease treatment. [15]

6. Induced Pluripotent Stem Cells

Induced Pluripotent Stem Cells (iPSCs) have revolutionized regenerative medicines. They're like versatile human embryonic stem cells, without the ethical concerns. iPSCs are used for drug testing and disease modeling, and they're sourced easily from patients. They've helped study heart, brain, liver diseases, and more. Scientists are figuring out how to use them effectively. iPSCs have huge potential in the medical field. [16]

ROLE AND FUNCTIONAL DIVISION:

Table 2: Role & Functions Based on Types of Cell.

Types Of Stem Cell Therapy	Functional Divisions
1. Embryonic Stem Cells (ESCs):	-Derived from the inner cell mass of a blastocyst (early embryo). - Placed in a culture dish to grow and divide. - Can differentiate into any cell type in the body. - Ethical concerns due to their source (often from in vitro fertilization).
2. Somatic or Adult Stem Cells:	- Found in various tissues after development The function is to repair, grow, and replace cells. - Limited differentiation options compared to ESCs. -Examples include mesenchymal, neural, hematopoietic, and skin stem cells.
3. Mesenchymal Stem Cells:	-Commenced in bone marrow and other tissues. - Can transform into bone, cartilage, and fat cells. - Act pluripotent, capable of various germ layer specializations.
4. Neural Stem Cells:	- Bring about to nerve cells and supporting cells -Include oligo-dendrocytes and astrocytes.
5. Haematopoietic Stem Cells:	- Develop various blood cells: red, white, and platelets.
6. Reprogramming Adult Stem Cells:	-Adult stem cells can be turned back into a pluripotent state. - Done through techniques like nucleus transfer or cell fusion.

Table 3: Role & Functional Division Based on Potency. [18]

Types of Stem Cell	Functional Divisions
1. Totipotent Cells	-Can produce all cells of the body and extraembryonic tissues. -Earliest stage post-fertilization.
2. Pluripotent Cell	-Can form all cells of the body. -Obtained from inner cell mass of blastocyst.
3. Multipotent Cell	-Can separate into various cells within a specific tissue.
4. Oligo potent/Omnipotent Cells	-Form only a few or one type of cell in a tissue. Each type has different capabilities in forming different cell types.

FROM CONCEPT TO PRECLINICAL STUDIES:

1. Idea to Preclinical Study:

- Researchers get an idea for stem cell treatment.

- Choose a target disease and understand its causes.

- Stem cells can counter disease mechanisms.

2. Preclinical Studies:

- Test the idea's potential and safety in animals.

- In vitro (controlled environment) and in vivo (real conditions) studies.

- Aim: Gather evidence for clinical study.

3. Preclinical Study Steps:

- Validate and understand the treatment's effects.

- Find safe initial dosage and administration.

- Check for potential activity and toxicity.

- Test for special toxicities (genetic, carcinogenic, etc.).

- Decide whether to continue development.

In short, from idea to animal testing, researchers ensure their stem cell treatment is effective, safe, and ready for clinical study.

IN-VIVO AND IN-VITRO STUDIES:

Before moving to clinical trials, stem cell therapy ideas undergo comprehensive in vitro and in vivo studies. In vitro experiments manipulate biological conditions using genetic mutations, and drug testing, and observe changes in living cells. However, they might not fully mimic the complex in vivo environment. In vivo experiments, often conducted in rodents due to their similarities to humans, help overcome these limitations by providing more relevant insights.

Ethical considerations in animal studies are crucial. Key factors like cell type, dose, administration route, safety, and efficiency are vital in both in vitro and in vivo studies, guiding the preclinical phase before potential clinical applications. [19]

MERITS & DEMERITS:

A. Merits

1. Adult stem cells experience minimal rejection.

Adult stem cells exhibit minimal rejection rates. Treatment avenues can be crafted using these cells sourced from each patient. These cells can be converted into diverse therapies with a diminished risk of rejection due to their origin in the patient. Even when utilizing familiar umbilical cord blood cells for treatment creation, the likelihood of rejection remains notably low. This reduces the necessity for immunosuppressant regimens to uphold a favorable future quality of life.

2. Certain stem cells can be converted into pluripotent stem cells.

Certain types of stem cells can be converted into pluripotent stem cells. By applying iPS reprogramming factors, adult stem cells can be reprogrammed and turned into pluripotent stem cells. This transformation enables them to differentiate into various cell types, such as mesoderm, endoderm, or ectoderm cells. This method offers the potential advantages of embryonic stem cell lines for medical applications, eliminating the necessity to harm embryos for cell retrieval.

3. There are many available treatment choices for stem cells.

Stem cell therapy is primarily employed for treating conditions like leukemia and lymphoma through bone marrow transplants. In Canada, the use of Prochymal has gained conditional approval to address graft vs. host disease in steroid-resistant children. Additionally, Holoclar offers potential relief to individuals with severe limbal deficiencies caused by eye burns. In the US, the FDA has approved five hematopoietic cord blood treatments.

4. This research illuminates human life's workings.

Stem cell research enables us to grasp cell functioning, aiding comprehension of illnesses. This insight can lead to novel treatments, potentially enhancing life expectancy, preventing diseases, and cutting medical expenses.

5. Stem cells offer limitless potential due to their regenerative properties.

the ability to cultivate replacement organs for failing ones or regrow lost limbs using lab-grown replacements. Stem cell research holds boundless potential, from enhancing mental health to boosting insulin production, mending heart muscles, fixing torn ligaments, and combating illnesses like cancer. Embryonic stem cells offer similar possibilities, addressing genetic disorders and birth defects, ultimately enabling happier, healthier lives for more individuals.

B. Demerits

1. Rejection rates can be high for embryonic stem cells.

Embryonic stem cell treatments can lead to future health issues, including high rejection rates and tumor development. Some stem cells don't respond as expected to activation signals.

2. Detecting any type of stem cell can be a challenging process.

Embryonic stem cells are collected after growing embryos in a culture. It takes months for these cells to grow sufficiently for therapy. Obtaining adult stem cells, like from bone marrow, can be very painful and challenging, especially for those far from a suitable facility. This adds logistical complications.

3. Stem cell treatments lack established proof of efficacy.

Currently, stem cell treatments are in an experimental phase. While there's potential for success, uncertainty remains. The most successful therapy is hematopoietic stem cell transplantation (HSCtx), boasting a 90% effectiveness with around 50,000 yearly transplants.

4. Conducting stem cell research is an expensive endeavor

In the US, an approved stem cell treatment costs around $10,000, with some clinics lowering it by 20%. Internationally, a treatment can reach $100,000. Harvesting embryo cells costs up to $2,000, while adult stem cell procedures could add several thousand dollars. Insurance and government benefits usually don't cover experimental stem cell treatments. [20]

Controversies Regarding Stem Cell Therapy:

Stem cell research, particularly using human embryonic stem cells, raises ethical concerns due to embryo destruction and potential benefits. Three main ethical views exist:

1. Opponents consider embryos as human beings with full moral status. Destroying them for others' benefit violates their rights.

2. Some view early embryos as equivalent to other body cells, needing no special protection.

3. Others believe embryos lack full moral status and an absolute right to life. Protection may be balanced against research benefits.

Additionally, there's a distinction between cloning for reproduction and therapy. Some advocate banning all cloning, while others differentiate. Ethical disagreements persist, hindering policies for health and progress due to differing viewpoints. [21]

APPLICATIONS:

A. Hematologic Malignancies:

1. Acute Myeloid Leukaemia (AML)

Leukemic stem cells (LSCs) are central to relapsed and refractory illness, exhibiting self-renewal, proliferation, differentiation, immune evasion, and drug resistance via distinct methods. [22]

2. Acute Lymphoblastic leukemia (ALL)

Allogeneic hematopoietic stem cell transplantation using a strong pre-treatment plan is regarded as the most effective treatment after initial remission for adult acute lymphoblastic leukemia (ALL). [23]

3. Chronic Myeloid Leukaemia (CML)

Tyrosine kinase inhibitors (TKIs) have mostly replaced SCT as the primary treatment for chronic myeloid leukemia (CML), but SCT is still considered for certain cases. SCT can be improved with pre-transplant TKIs, specific regimens, monitoring, and relapse strategies. [24]

4. Multiple Myeloma

For eligible just recently identified multiple myeloma (MM) patients, autologous stem cell transplantation (auto-SCT) has been the established treatment approach. [25]

5. Myelodysplastic Syndromes (MDS)

Allogeneic hematopoietic stem cell transplantation (HCT) stands as the sole effective treatment for Myelodysplastic syndrome (MDS), providing a potential cure. [26]

B. Lymphomas:

1. Hodgkin's Lymphoma

Autologous stem cell transplant works well for relapsed Hodgkin's lymphoma if pre-transplant chemo is effective. Treatment-resistant cases have a poorer outlook. Also, low haemoglobin at diagnosis affects post-transplant survival. [27]

2. Non-Hodgkin's Lymphoma

For patients with degenerative or refractory NHL, using a salvage chemotherapy regimen followed by high-dose chemotherapy consolidation and autologous stem cell transplant can lead to a potential cure. [28]

C. Bone Marrow Failure Syndromes:

1. Aplastic Anaemia (AA)

hESC therapy offers promise for treating aplastic anemia (AA). Research demonstrated significant patient improvement after hESC treatment with no negative effects. This therapy appears both safe and effective for AA patients. [29]

2.Paroxysomal Nocturnal Hemoglobinuria (PNH)

PNH is a rare disorder where cells lack CD55 and CD59 proteins, causing complement-mediated cell lysis. Allogeneic hematopoietic stem cell transplantation is the sole curative option. [30]

1. Fanconi Anaemia (FA)

Allogeneic bone marrow transplant is the sole cure for Fanconi Anemia (FA), but progress in stem cell and gene therapy offers potential alternative treatments. [31]

2. Pure Red Cell Aplasia (PRCA)

A recognized treatment approach has not been established for pure red cell aplasia following significant ABO-incompatible hematopoietic stem cell transplantation (HSCT). [32]

D. Genetic Metabolic Disorders:

1. Hurler Syndrome (HS)

Hurler Syndrome (HS) is a condition with serious health issues and early childhood death. Hematopoietic stem cell transplantation (HSCT) can lead to long-term survival. [33]

2. Adrenoleukodystrophy

Allogeneic hematopoietic stem cell transplantation (HSCT) is the sole treatment for Adrenoleukodystrophy (ALD), leading to lasting quality of life. [34]

3. Gaucher Disease (GD)

Hematopoietic Stem Cell Transplantation is a treatment with the potential to permanently cure Gaucher disease by using hematopoietic stem cells. [35]

E. Genetic Immune System Disorders

1. Severe Combined Immunodeficiency (SCID)

HSCT stands as the primary curative choice for the majority of youngsters affected with critically combined immunodeficiency disease (SCID). [36]

2. Chronic Granulomatous Disease (CGD)

Allogenic Hematopoietic stem cell transplantation (HSCT) is the main cure for CGD, a condition caused by faulty NADPH-oxidase enzyme. It replaces damaged stem cells to treat the disease. [37]

F. Autoimmune Disorders:

1. Multiple sclerosis (MS)

mesenchymal stem cells (MSC's), neural precursor/stem cells (NSC's), induced pluripotent stem cells (iPSC's),and cell replacement therapy could be an applicable prospective for immunomodulatory treatment in multiple sclerosis. [38]

2. Rheumatoid Arthritis (RA)

Mesenchymal Stem Cells (MSC's) can treat autoimmune diseases and aid in stem cell therapy. RA, a chronic autoimmune disorder, damages synovium, causing pain, inflammation, and cartilage/bone deterioration. [39]

G. Neurological Disorders:

1. Parkinson's Disease (PD)

Transplanting dopamine-producing cells into the brain can help replace lost neurons in Parkinson's patients, improving dopamine communication and potentially treating the condition. [40]

2. Alzheimer's Disease (AD)

Alzheimer's disease is a neurodegenerative disorder that leads to memory issues. Stem cell treatments, such as induced pluripotent stem cells, neural stem cells, and mesenchymal stem cells, hold promise for Alzheimer's disease therapy.[41]

3. Traumatic brain injury (TBI)

These stem cells, with their potential to transform into nerve cells and release neurotrophic factors, appear promising for treating traumatic brain injuries. [42]

4. Spinal Cord Injuries (SCI)

Spinal Cord Injury (SCI) leads to the loss of nervous tissue and associated motor/sensory function. Stem cells can be guided to become neurons/glial cells in the lab, potentially replacing the lost neural cells post-SCI. [43]

H. Cardiovascular diseases:

1. Ischemic Heart Disease (myocardial infarction)

Various cell types, such as BM-derived cells, EPCs, UCB stem cells, CSCs, ESCs, and induced pluripotent stem cells, have been utilized for cardiac repair in ischemic heart diseases including Myocardial infarction. [44]

2. Congestive Heart Failure (CHF)

Both bone marrow-obtained mononuclear cells and mesenchymal stem cells (MSCs) have been separately used to treat congestive heart failure (CHF). [45]

I. Diabetes:

Type 1 Diabetes Mellitus

Stem cells, like Mesenchymal Stem Cells (MSCs) preposition outside of sources like bone marrow and cord blood, offer advantages for T1DM treatment. Pluripotent stem cells can become β-cells, boosting insulin secretion. [46]

Type 2 Diabetes Mellitus

Lately, there has been substantial research interest in utilizing mesenchymal stem cells (MSCs) from different adult tissues as a potential treatment for diabetes. These MSCs can stimulate the regeneration of insulin-producing β-cells in the pancreatic islets. [47]

J. Liver Diseases:

1. Acute Liver Failure

Various types of stem cells, such as MSCs, LSCs, ESCs, iPSCs, and PBSCs, can improve liver damage and potentially treat liver diseases. [48]

K. Lung Diseases:

1. Chronic Obstructive Pulmonary Disease (COPD)

Utilizing stem cells for therapy holds significant promise in addressing degenerative lung conditions, showcasing the substantial potential for positive outcomes. [49]

2. Cystic Fibrosis (CF)

Cell-based therapeutic strategies for cystic fibrosis have emerged as a viable treatment option that holds the promise of eventually providing a cure for the condition. [50]

3. COVID-19

Patients with COVID-19 have undergone transplantation of mesenchymal stem cells (MSCs) derived from human umbilical cords (UC-MSC).[51]

L. Gastrointestinal Disorders:

1. Crohn's Disease

Stem cells provide a promising way to help people with Crohn's disease by changing how their immune system behaves and how their body heals. [52]

2. Graft-versus-Host Disease (GVHD)

Ongoing research suggests that MSCs might have a significant role in the future for managing Graft-versus-Host Disease (GVHD) by controlling inflammation. [53]

GLOBAL MARKET OVERVIEW:

In 2022, the global market size for stem cell therapy was valued at approximately USD 11.22 billion. Projections indicate that it could attain a value of about USD 31.41 billion by 2030, with a compound annual growth rate (CAGR) of roughly 13.73% expected from 2023 to 2030. Furthermore, estimates suggest that the market could grow to USD 24.29 billion by 2028.By Product:

- Adult Stem Cells (ASCs) had an 85.9% revenue share in 2021.

- Induced pluripotent stem cells (iPSCs) are projected to experience a compound annual growth rate (CAGR) of 9.5% between 2022 and 2030.

By Application:

- Regenerative Medicine accounted for 91% of revenue share in 2021.

- Drug Discovery and Development application is projected to grow at a 9.5% CAGR from 2022 to 2030.

By Therapy:

- Allogenic Stem Cell Therapy held a market share of 58.5% in 2021.

By Region:

- North America had the largest market share at 53% in 2021.

- Asia Pacific is predicted to grow at a 9.2% CAGR between 2022 and 2030.

Prominent Participants in the Worldwide Stem Cell Market.

1. Thermo Fisher Scientific

2. Brainstorm Cell Therapeutics

2. Stemcell Technologies Inc.

3. Gamida Cell

4. PLURISTEM THERAPEUTICS

5. Cellular Engineering Technologies Inc.

6. STEMCELL Technologies Inc.

7. CellGenix GmbH

8. PromoCell GmbH

Recent Developments:

1. In July 2023, PromoCell introduced the 'PromoExQ MSC Growth Medium XF,' designed to meet EXCiPACT GMP certification standards, and specifically tailored for the expansion of human MSCs in GMP-regulated environments.

2. April 2023 - Gamida Cell: FDA approves allogeneic cell therapy 'Omisirge' for hematologic malignancies in patients aged 12 and above, based on a global Phase 3 study.

3. In March 2023, Cellular Engineering Technologies (CET) obtained exclusive authorization to utilize immortalized human stem cells from the John Paul II Medical Research Institute, which aims to tackle hurdles associated with iPSC-dependent cell replacement therapy.

4. January 2023 - BrainStorm Cell Therapeutics: Donates biospecimens from NurOwn's Phase 3 ALS trial to the research community, including serum and cerebrospinal fluid samples.

5. June 2022 - STEMCELL Technologies: Partners with PBS Biotech to provide the PBS-MINI Bioreactor for scaling human pluripotent stem cell cultures using TeSR media.

6. April 2022 - STEMCELL Technologies Canada: Collaborates with Applied Cells for an efficient cell separation solution combining EasySep kits with Applied Cells' MARS platform.7.March 2022 - Cellular Engineering Technologies: Granted US patent for virus- and oncogene-free iPSC technology, supported by SBIR grant for commercialization. [54,52]

CONCLUSION:

In summary, the field of stem cell therapy has witnessed significant progress and holds great promise for medical advancement. Stem cells' unique ability to regenerate damaged tissues and their diverse applications have been explored in this review. While ethical and technical challenges persist, the therapeutic potential across various diseases is evident. The global stem cell therapy market is growing, driven by research, regulatory approvals, and investment. Recent developments by key players underscore the ongoing innovation in this

field. Overall, while obstacles remain, ongoing research in stem cell therapy offers hope for transformative treatments and improved quality of life for patients globally.

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