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Overview of Stem Cell Therapies in Immune System Disorders

Longfei Zhao *

School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, 4072 QLD, Australia

* Corresponding Author Email: s4851698@uq.edu.au

Abstract. The advent of stem cell technology signifies a novel era in the field of medicine, providing revolutionary therapies for a range of diseases, including immune system disorders. Stem cells have a remarkable ability to regenerate and differentiate into many types of cells, which makes them highly promising for the repair of damaged tissues and organs. The objective of this study is to investigate the capacity of stem cell treatment in addressing immune system disorders. The article examines recent advancements and uses of several types of stem cells in regulating the immune response, restoring injured tissues, and offering long-term solutions for treating immunological-mediated diseases. The study encompasses an extensive examination of stem cell differentiation, immune system disorders, and in-depth case studies that showcase the achievements and difficulties encountered when utilizing stem cells to treat conditions such as rheumatoid arthritis, systemic lupus erythematosus, immune thrombocytopenia, and Crohn's disease. The paper also investigates the methods via which stem cells execute their therapeutic effects, including immune regulation and tissue restoration. The conclusion highlights the substantial advancements achieved in stem cell research and its auspicious prospects in personalized medicine and regenerative therapeutics.

Keywords: Stem cell therapy, immune system disorders, regenerative medicine.

1. Introduction

The emergence of stem cell technology marks the beginning of a new age in medicine, offering groundbreaking treatments for a wide range of illnesses, including those that impact the immune system. Stem cells possess an extraordinary capacity to renew themselves and transform into diverse types of cells, making them very promising for the restoration of damaged tissues and organs. The prospect of using several forms of stem cells, including embryonic stem cells (ESCs), adult stem cells (ASCs), and induced pluripotent stem cells (iPSCs), has sparked considerable research enthusiasm for their classification and utilization in medical contexts.

Embryonic stem cells, obtained from the inner cell mass of the blastocyst, have the potential to differentiate into any cell type in the organism, making them fully pluripotent. Adult stem cells, although limited by their multipotency, have been identified in various tissues, such as the bone marrow and brain, and are instrumental in the body's routine maintenance and repair processes [1]. Induced pluripotent stem cells, generated by reprogramming somatic cells, have emerged as a powerful tool for personalized medicine, sidestepping the ethical dilemmas posed by ESCs while offering a vast array of therapeutic possibilities [2].

Stem cells have a wide range of applications in medicine, going beyond their ability to regenerate tissue. They are essential for creating models of diseases, evaluating the effects of drugs, and serving as a foundation for genetic therapies. For instance, iPSCs have been utilized to simulate the pathophysiology of neurodegenerative disorders, offering an understanding of disease mechanisms and possible targets for therapeutic development [3]. Furthermore, the practical use of stem cells has made substantial progress, with hematopoietic stem cell transplantation now becoming a conventional therapy for several types of blood cancers.

Immunological system disorders encompass a wide range of ailments that result from abnormal immunological responses, including autoimmune diseases, immunodeficiencies, and hypersensitivity reactions. Autoimmune diseases such as rheumatoid arthritis and type 1 diabetes result from the immune system erroneously attacking the body, while immunodeficiencies, either congenital or acquired, like in the case of HIV/AIDS, compromise the body's ability to fend off infections [4]. Traditional therapies for these conditions typically include immunosuppression, which, although successful in alleviating symptoms, can result in a multitude of adverse reactions and heightened vulnerability to infections.

This research aims to clarify the potential of stem cell therapy in treating immune system illnesses. This study will review the latest breakthroughs and applications of stem cells in modulating the immune response, repairing damaged tissues, and providing a sustainable approach to treating immunological-mediated illnesses. The subsequent parts will provide a comprehensive analysis of the many categories of stem cells, their characteristics and potential, the fundamental principles of stem cell differentiation, and a summary of the immune system and its ailments.

We will examine the historical backdrop of stem cell therapies, starting from the initial bone marrow transplants to the present state-of-the-art methods utilizing induced pluripotent stem cells (iPSCs). The paper will provide detailed case studies that highlight the successes and challenges of using different types of stem cells to treat immune system disorders. These include embryonic stem cells (ESCs) for immunodeficiency, MSCs for autoimmune diseases, and iPSCs for various inflammatory conditions.

Furthermore, the paper will delve into the mechanisms by which stem cells exert their therapeutic effects, be it through direct differentiation into functional immune cells or by modulating the immune response to alleviate symptoms and prevent disease progression.

2. Stem cells

Stem cells are essential in regenerative medicine because of their distinct capacities for self-renewal and differentiation into diverse cell types. Various categories of stem cells exist, each possessing unique attributes and uses.

2.1. Types of stem cells

2.1.1. Embryonic stem cells (ESCs)

Source and Properties: ESCs are obtained from the inner cell mass of blastocysts, which is the pre-implantation phase of development. These cells possess pluripotency, indicating their capacity to undergo differentiation into any cell type found in the body [5].

Ethical Considerations: ESCs may give rise to ethical issues since the extraction procedure necessitates the killing of the embryo. As a result, there have been discussions and strict rules concerning their utilization in research and treatment [6].

2.1.2. Adult stem cells (ASCs)

ASCs are a type of stem cell that may differentiate into many cell types. They can be found in different tissues, including bone marrow (where they are called hematopoietic stem cells) and fat tissue (where they are called mesenchymal stem cells). They have a vital function in the body's maintenance and repair processes. Hematopoietic stem cells are utilized in bone marrow transplants for the treatment of blood illnesses such as leukemia, whereas mesenchymal stem cells are being investigated for their capacity to repair bone, cartilage, and other tissues [7].

Advantages: ASCs are less contentious compared to ESCs due to their ability to be obtained from the patient's own body. This reduces the likelihood of immunological rejection and mitigates ethical concerns [8].

2.1.3. Induced pluripotent stem cells (iPSCs)

iPSCs are created by transforming somatic cells, including skin cells, into a pluripotent state. This is originally achieved through the activation of transcription factors, such as Oct4, Sox2, Klf4, and c-

Myc. The reprogramming technology developed by Shinya Yamanaka enables the production of stem cells that are tailored to individual patients, facilitating the advancement of personalized medicine, disease modeling, and drug testing [9].

Advantages: iPSCs bypass the ethical issues linked to ESCs and offer potential for autologous cell treatments, which are customized to each patient, thus reducing the likelihood of immunological rejection [10].

2.2. Differentiation process

The process of stem cell differentiation is controlled by an intricate interaction between signaling pathways and transcription factors. Crucial pathways such as Wnt, Notch, and Hedgehog interact with others to regulate gene expression and cellular activity. Wnt signaling plays a vital role in the process of stem cell self-renewal, whereas Notch signaling affects the determination of cell destiny [11, 12].

2.3. Stages from stem cells to defined cells

The differentiation process involves several stages:

Cell fate commitment: stem cells acquire cues that determine their cell fate to a certain lineage.

Proliferation: progenitor cells undergo rapid cell division, increasing the number of cells that are predetermined to perform a specific role.

Differentiation: progenitor cells undergo further specialization, acquiring the characteristics and functions of mature cell types.

Stem cell research has been greatly transformed by the latest developments in genome editing tools, such as CRISPR/Cas9. These technologies provide accurate manipulation of genes in stem cells, empowering scientists to comprehend and potentially rectify genetic abnormalities that give rise to diseases. Consequently, the possible uses of stem cells in the treatment of various ailments are constantly growing, signaling the beginning of a new age in personalized medicine and regenerative therapies [13, 14].

3. Immune system disorders

The immune system is an intricate network comprising cell level, tissue level, and organ level that collaborate to protect the body from detrimental microorganisms and diseases. The system consists of two primary components: the innate immune system, which offers immediate but non-specific defense, and the adaptive immune system, which provides long-lasting and protection. Although the immune system is generally efficient, it may lead to a range of immunological-related diseases when functional abnormalities occur.

3.1. Common immune system diseases

3.1.1. Autoimmune Diseases

Autoimmune illnesses arise when the immune system mistakenly identifies the body's own tissues as hazardous intruders and attacks them. Chronic inflammation and tissue damage occur because of this misguided immune response. Autoimmune illnesses, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), serve as examples.

Rheumatoid Arthritis (RA):

RA is a persistent inflammatory condition that mostly impacts the joints. The condition is defined by the immune system's assault on the synovium, which is the protective membrane surrounding the joints. This causes painful swelling, which can eventually result in bone erosion and joint deformity [15]. The pathogenesis of RA is characterized by an intricate interaction between genetic susceptibility and environmental influences. This results in the stimulation of self-reactive T cells and the generation of autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) [16].

Systemic Lupus Erythematosus (SLE):

SLE is a condition where the body's immune system mistakenly attacks various organs, such as the skin, joints, kidneys, and brain. SLE is characterized by the development of antinuclear antibodies (ANAs) that specifically attack the cell nucleus. The development of SLE is caused by a combination of hereditary factors, hormonal effects, and environmental triggers. This leads to the activation of B cells and T cells that attack the body's own tissues, causing inflammation and damage throughout the body [17].

3.1.2. Immune thrombocytopenia (ITP)

ITP is a medical condition caused by the immune system attacking platelets, resulting in a reduced number of platelets in the blood. This leads to a higher risk of bleeding and bruising. Within the context of ITP, the immune system generates antibodies that specifically target platelets, so designating them for elimination by the spleen. The exact cause of ITP is often unknown, but it can be triggered by infections, medications, or other autoimmune conditions [18]. The symptoms of ITP encompass facile bruising, petechiae (little red spots on the skin), and protracted bleeding from incisions. Internal bleeding can develop in severe situations, presenting substantial health hazards [19].

3.1.3. Inflammatory diseases

Chronic inflammation is a distinguishing characteristic of numerous disorders that are related to the immune system. Continual inflammation can result in harm to tissues and contribute to a range of illnesses, such as Crohn's disease.

Crohn's Disease: Crohn's disease is an inflammatory bowel disease (IBD) characterized by inflammation of the digestive tract, resulting in abdominal pain, excessive diarrhea, exhaustion, weight loss, and malnutrition. Crohn's disease-induced inflammation can impact several regions of the gastrointestinal system, typically affecting the small intestine and the initial segment of the colon. The precise etiology of Crohn's disease remains uncertain. However, it is believed to result from a complex interplay of genetic, environmental, and immunological variables. The immune system's reaction to the bacteria in the gut is extremely important in the development of Crohn's disease. When the immune system responds abnormally, it causes ongoing inflammation and harm to the tissues [20].

3.2. Current Therapies' Limitations

Despite advances in the treatment of immune system diseases, current therapies have several limitations:

3.2.1. Medication Side Effects

Several drugs employed in the treatment of immune system disorders, such as corticosteroids and immunosuppressants, can induce notable adverse effects. These potential side effects encompass weight gain, hypertension, diabetes, heightened susceptibility to infections, and osteoporosis. Prolonged usage of these medications can result in significant health consequences, which can make it difficult to properly control the disease [21].

3.2.2. Lack of therapeutic effect

A considerable proportion of patients fail to attain full remission with current therapy. For example, in RA, whereas TNF inhibitors have enhanced results, a significant number of patients nevertheless face ongoing disease activity and gradual deterioration of their joints [22].

3.2.3. High Recurrence Rates

Several immune-related disorders exhibit a chronic and relapsing nature. Patients with ITP frequently encounter repeated instances of reduced platelet levels, even following an initial effective therapy. This requires continuous monitoring and frequent treatments, which can be demanding and impact the quality of life [19].

4. Applications of Stem Cell Therapy in Immune System Diseases

Stem cell therapy has become a hopeful treatment for a range of immune system disorders. This section examines the historical background and progress of stem cell research, showcases examples of its application in therapy, and investigates the mechanisms involved in stem cell therapy, such as immune regulation and tissue restoration.

4.1. History and Development

Milestones in Stem Cell Research:

Stem cell research has made significant strides since its inception. The discovery of hematopoietic stem cells (HSCs) in the 1960s marked the beginning of modern stem cell research. HSCs, which can differentiate into all types of blood cells, have revolutionized the field of medicine by bone marrow transplants. These transplants have now become a widely accepted and established treatment for blood malignancies and other illnesses of the blood [23].

During the 1980s and 1990s, researchers discovered and extracted mesenchymal stem cells (MSCs) from bone marrow. These cells have the ability to transform into bone, cartilage, and fat cells [24]. The discovery of induced pluripotent stem cells (iPSCs) by Shinya Yamanaka in 2006 brought about a significant change in the field of stem cell research. It enabled the transformation of adult cells into a condition where they possess the ability to develop into any type of cell in the body [9]. This breakthrough facilitated the production of stem cells that are tailored to individual patients, therefore resolving the ethical concerns linked to embryonic stem cells (ESCs).

Early Clinical Trials:

Initial clinical trials were primarily concerned with assessing the safety and viability of stem cell therapy. For instance, hematopoietic stem cell (HSC) transplants have effectively been employed in the treatment of leukemia [25]. The experiments provided evidence that stem cells could be delivered without risk and suggested their potential for therapeutic use.

4.2. Case Studies in Therapy

4.2.1. Autoimmune Diseases

Stem cell research has primarily focused on autoimmune illnesses, which occur when the immune system erroneously targets the body's own tissues.

Rheumatoid Arthritis (RA):

MSCs have been investigated for their ability to modify the immune response in RA. A study provided evidence that MSCs can inhibit inflammatory reactions and enhance the clinical manifestations in individuals with RA [26]. Nevertheless, there are still obstacles to optimize the distribution and guarantee the long-term effectiveness of therapeutic effects.

Systemic Lupus Erythematosus (SLE):

HSC transplantation has been employed to restore the immune system in cases of severe SLE. In previous studies, researchers found that autologous hematopoietic stem cell transplantation resulted in extended periods of remission in individuals with treatment-resistant SLE. Nonetheless, the procedure carries risks, including infection and graft-versus-host disease (GVHD).

4.2.2. Immune Thrombocytopenia (ITP)

ITP is defined as thrombocytopenia caused by the immune system's destruction of platelets. Conventional therapies consist of corticosteroids and intravenous immunoglobulins, which frequently offer only transient alleviation. Stem cell treatment presents a promising and enduring solution.

Case Studies:

Multiple case reports have demonstrated that infusions of MSCs can enhance platelet counts and alleviate bleeding in individuals with ITP. An example is a study which showed that MSC therapy resulted in long-lasting improvement in a specific group of ITP patients. The precise mechanisms are currently under investigation. However, it is believed that MSCs can regulate the immune response and facilitate tissue regeneration.

4.2.3. Inflammatory Diseases

Chronic inflammatory disorders such as Crohn's disease and multiple sclerosis (MS) are incapacitating conditions that have few therapy alternatives.

Crohn's Disease:

MSCs have been used to treat refractory Crohn's disease with promising results. A study found that Stem cell transplantation is a beneficial adjunctive treatment for CD [27]. The anti-inflammatory properties of MSCs, along with their ability to repair damaged intestinal tissues, contribute to these therapeutic effects.

Multiple sclerosis (MS):

HSC transplantation has demonstrated promise in stopping the progression of multiple sclerosis. Research reported that the transplantation of autologous HSC resulted in sustained improvement in individuals with aggressive MS[28]. The treatment functions by eliminating the malfunctioning immune system and facilitating the formation of a new, robust immune system.

4.3. Mechanisms of Stem Cell Therapy

4.3.1. Immune Modulation

Stem cells, specifically MSCs, possess strong immunomodulatory properties. They have the ability to inhibit the growth of T cells and B cells, decrease the secretion of pro-inflammatory cytokines, and boost the function of regulatory T cells (Tregs) [29]. This immune modulation helps to restore immune tolerance and reduce autoimmune attacks.

T-Cell Regulation:

MSCs secrete factors like prostaglandin E2 (PGE2) and indoleamine 2,3-dioxygenase (IDO), which inhibit the activation and proliferation of T cells [30]. They also promote the generation of Tregs, which play a crucial role in maintaining immune homeostasis.

B-Cell Regulation:

MSCs can modulate B-cell function, reducing antibody production and altering the cytokine profile to favor anti-inflammatory responses [31].

4.3.2. Tissue Repair

In addition to immune modulation, stem cells contribute to tissue repair and regeneration.

Paracrine Effects:

Stem cells secrete a diverse range of growth factors, cytokines, and extracellular vesicles that facilitate tissue regeneration. These substances promote the activation of cells already present in the body, decrease programmed cell death, and improve the process of restoring injured tissues[32].

Direct Differentiation:

Stem cells can directly transform into the specific cell types required for tissue regeneration in certain situations. For example, MSCs have the ability to transform into chondrocytes, osteoblasts, and adipocytes, which helps in the regeneration of cartilage, bone, and fat tissues[33].

5. Challenges and Prospects of Stem Cell Therapy

Stem cell treatment has great potential for treating various diseases, but it also has numerous notable obstacles. One of the main technological challenges is to ensure the secure and efficient incorporation of stem cells into the tissues of patients. Immune rejection, uncontrolled cell proliferation, and possible tumorigenicity are major hazards that need to be considered.

Recent research has made significant advancements in tackling these difficulties. The development of genome editing technologies, specifically CRISPR/Cas9, has facilitated accurate genetic alterations to enhance the safety and effectiveness of stem cells [14] Moreover, the development of novel techniques to induce pluripotency is continuously improving the therapeutic capabilities of stem cells [9]. As research continues to advance, stem cell therapy is poised to become a cornerstone of modern medicine, transforming the landscape of therapeutic interventions and patient care.

The obstacles and potential of stem cell therapy are of utmost importance to our debate. Although the science holds great promise, it is not without its challenges, including the possibility of cancer development, ethical concerns, immune rejection, and the intricacies of manufacturing and obtaining regulatory approval. Nonetheless, Recent advancements in research indicate a promising future. The development of genome editing technologies, such as CRISPR/Cas9, has created opportunities for the secure and effective utilization of stem cells, potentially resolving existing challenges. [13].

The potential ramifications for patients and the healthcare system are substantial, as stem cell therapies have the potential to provide more precise, efficient, and long-lasting treatments in comparison to traditional approaches. The study will analyze the cost-effectiveness of these treatments, the impact on patient quality of life, and the wider implications for healthcare delivery.

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