



STEM CELL THERAPY-A NEW TREATMENT METHOD

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DOI: <https://doi.org/10.5281/zenodo.17233101>

Article Received on 25/04/2023

Article Revised on 15/05/2023

Article Accepted on 05/06/2023

1. INTRODUCTION

Despite the progress in medical science, there still exist various diseases in the world for which there is no suitable treatment. People affected by incurable disorders typically use treatment methods intended to decrease the somatic and psychological symptoms and, in these situations, the physician offers treatment methods only to manage the disease, not treat it. Therefore, researchers are attempting to develop new treatment methods to not only control the symptoms of, but also to treat those diseases for which no cure is available at present.

Regenerative medicine is considered a promising new source of treatment for untreatable diseases in modern science.^[1] Regenerative medicine is a multidisciplinary field including cell biology, genetic, biomechanics, material science, and computer science^[2,3], the ultimate target of which is returning normal function to defective cells and tissues.^[4] Since the discovery of stem cells and the spread of awareness regarding their unique properties, they have been defined as therapeutic agents for organ and tissue repair, and so are widely considered good candidates for regenerative medicine, due to their many potential applications.^[5] Regenerative medicine is now regarded as an alternative to traditional drug-based treatments by researchers who study its potential applications in various diseases, including degenerative diseases, among others.^[6]

Stem cells are a group of immature cells that have the potential to build and recover every tissue/organ in the body due to their unique proliferative, differentiation, and self renewal abilities.^[7] Stem cells provide therapeutic effects which improve physical development by regenerating damaged cells to assist in organ recovery. Relying on the natural abilities of stem cells, researchers have used their biological mechanisms for stem-cell-based therapy. The mechanisms of action through which stem cells can promote the regeneration of tissue are diverse, including

- (1) inhibition of inflammation cascades.^[8,9]
- (2) reduction of apoptosis^[10,11],
- (3) cell recruitment^[12,13],
- (4) stimulation of angiogenesis^[14,15], and
- (5) differentiation.^[16]

Stem cell-based therapy

Stem cell-based therapies are defined as any treatment for a disease or a medical condition that fundamentally involves the use of any type of viable human stem cells including embryonic stem cells (ESCs), iPSCs and adult stem cells for autologous and allogeneic therapies.^[17]

However, the complexity of stem cell-based therapies often leads researchers to search for stable, safe and easily accessible stem cells source that has the potential to differentiate into several lineages. Thus, it is of utmost importance to carefully select the type of stem cells that is suitable for clinical application.^[18]

Therapeutic translation of stem cell research

With the rapid increase witnessed in stem cell basic research over the past years, the relatively new research discipline "Translational Research" has evolved significantly building up on the outcomes of basic research in order to develop new therapies.^[19]

There are more than 3,000 trials involving the use of adult stem cells registered in WHO International Clinical Trials Registry. Additionally, initial trials involving the new and appealing iPSCs based therapies are also registered. In fact, the first clinical attempt employing iPSCs reported successful results in treating macular degeneration.^[20]

TYPES OF STEM CELL

1) Mesenchymal Stem Cells (MSCs)

MSCs are lineage-committed cells that divide into mesenchymal systems, primarily fatty cells, chondrocytes, and osteocytes. The biggest characteristics of MSCs are their immunosuppressive functions, which prevent the proliferation of activated T cells through

immunosuppressive cytokine secretion and suppression of programmed cell death signaling. Due to this role, they have been spotlighted as a potential treatment for immune-related inflammation and disease.^[21]

2) Hematopoietic Stem Cells (HSCs)

HSCs can be differentiated into cells from all hematopoietic systems present in the bone marrow and chest glands, namely myeloid cells and lymphocytes. HSCs can be obtained at good levels from adult bone marrow, the placenta, and cord blood. Nevertheless, they have been shown to be an effective treatment method in various diseases, including leukemia, malignant lymphoma, and regenerative anemia, as well as congenital metabolism, congenital immunodeficiency, nonresponsive autoimmune disease, and solid cancer to date. Furthermore, HSCs are the only stem cell type approved for stem cell treatment by the Food and Drug Administration (FDA)^[22]

3) Embryonic Stem Cells (ESCs)

ESCs have established cell lines that can be maintained through in vitro culture. They are pluripotent cells that can be differentiated into almost any type of cell present in the body, and can be differentiated in vitro by adding external factors to the culture medium or by genetic modification.^[23]

4) Induced Pluripotent Stem Cells (iPSCs)

iPSCs are artificially created stem cells. These cells are made by reprogramming adult somatic cells such as fibroblast cells. They share many of the characteristics of ESCs, including self-renewability, pluripotent differentiation, and malformed species performance.^[24]

Stem cell-based therapy for neurodegenerative diseases (PDF2)

1) Parkinson's disease (PD)

PD is characterized by a rapid loss of midbrain dopaminergic neurons. The first attempt for using human ESC cells to treat PD was via the generation of dopaminergic-like neurons, later human iPSCs was proposed as an alternative to overcome ESCs controversies.^[25]

2) ALS

ALS is a neurodegenerative disease that causes degeneration of the motor neurons which results in disturbance in muscle performance. Based on these results, several planned/ongoing clinical trials are on the way. These trials mainly assess the safety of the proposed concept and have not proved clinical success to date. Notably, while pre-clinical studies have reported that cells derived from un-diseased individuals are superior to cells from ALS patients; most of the clinical trials attempted have employed autologous transplantation. This information may account for the absence of therapeutic improvement reported.^[26]

Stem cell-based therapies for treatment of diabetes

Pancreatic beta cells are destructed in type 1 diabetes mellitus, because of disorders in the immune system while in type 2 insulin insufficiency is caused by failure of the beta-cell to normally produce insulin. In both cases the affected cell is the beta cell, and since the pancreas does not efficiently regenerate islets from endogenous adult stem cells, other cell sources were tested. Pluripotent stem cells (PSCs) are considered the cells of choice for beta cell replacement strategies.^[27]

Stem cells in dentistry

Stem cells have been successfully isolated from human teeth and were studied to test their ability to regenerate dental structures and periodontal tissues. MSCs were reported to be successfully isolated from dental tissues like dental pulp of permanent and deciduous teeth, periodontal ligament, apical papilla and dental follicle.^[28]

Stem cells and tissue banks

The ability to bank autologous stem cells at their most potent state for later use is an essential adjuvant to stem cell-based therapies. In order to be considered valid, any novel stem cell-based therapy should be as effective as the routine treatment. Thus, when appraising a type of stem cells for application in cellular therapies, issues like immune rejection must be avoided and at the same time large numbers of stem cells must be readily available before clinical implementation. iPSCs theoretically possess the ability to proliferate unlimitedly which pose them as an attractive source for use in cell-based therapies.^[29]

CONCLUSIONS

In recent years, regenerative medicine has become a promising treatment option for various diseases. Due to their therapeutic potential, including the inhibition of inflammation or apoptosis, cell recruitment, stimulation of angiogenesis, and differentiation, stem cells can be seen as good candidates for regenerative medicine. Approximately 50% of clinical trials using stem cells take 2 to 5 years to complete. To minimize possible side effects, every new stem cell product should be approved for clinical marketing only after completing Phase I–IV clinical trials successfully. To develop new stem-cell-based medicine for the clinical market, researchers should follow the guidelines suggested by the relevant authorities. Through these well-controlled development processes, researchers can achieve safe and effective stem-cell-based therapies, thus brings their research ideas into the clinical field.

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