

# STEM CELL, STEM CELL BASED THERAPY AND IT'S PROMISING APPLICATION ON CHRONIC AND LIFE THREATENING DISORDERS: A REVIEW

## Abstract

In recent years, stem cell treatment has become a highly desirable and innovative field of study in science. There are high expectations for the development of treatment procedures. The idea of regenerative medicine—which involves harnessing the body's own stem cells and growth factors to heal tissues—may come to pass as fresh discoveries in basic science and preliminary clinical experiences have "teamed up" to create different approaches to treating the illness. Research on stem cells and the growing understanding of biological concepts in the regeneration of oral and dental tissues are expected to lead to a paradigm change in the treatment armament for dental and oral illnesses. This will lead to a fervent search for "biological solutions to biological problems." Early data from groundbreaking research has demonstrated the potential breakthrough that stem cells offer for a number of serious illnesses that have eluded current medical treatment. This book chapter's main focus are the identification of diverse stem cells and potential therapies derived from these cells.

**Keywords:** stem cell, types, stem cell therapy, regeneration

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## I. INTRODUCTION

Stem cell treatment has emerged as a very promising and cutting-edge area of scientific study in recent years. The treatment methods have evoked significant expectations. An overview of stem cells and possible treatments based on them is presented in this book chapter [1]. By controlling the culture and derivation of stem cells, stem cells are generated in the laboratory. In order to evaluate the characteristics of the stem cells, quality control and teratoma formation tests are essential. Culturing media and the methods of extraction are crucial to setting the right conditions for controlled differentiation. Due to their versatility, grapheme scaffolds and attention must be paid to extracellular vesicle-based therapeutics among stem tissue applications. For stem cell treatment to gain global acceptance, a number of challenges must be overcome. In modern medicine, this cutting-edge therapy provides hope for untreatable diseases by providing a wide range of possibilities [2].

## II. CLASSIFICATION OF STEM CELLS

Stem cells are unspecialized cells found in the human body. They have the capacity to self-renew in addition to differentiating into any type of cell in an organism. Both embryonic and adult stem cells contain stem cells [3]. The process of specialization involves several steps. The development potency of a unipotent stem cell decreases with each step, so it cannot differentiate into as many types of cells as a pluripotent stem cell [4]. To make understanding the following chapters easier, we will focus on stem cell classification in this chapter [5].

Totipotent stem cells being able of dividing and diversifying into cells of the entire organism. As a result of totipotency, cells are capable of forming both embryonic and extra-embryonic structures [6]. A zygote, which is created when a sperm fertilizes an egg, is a totipotent cell. These cells have the potential to produce a placenta or one of the three germ layers, depending on how they develop [7]. After about 4 days, the inner cell mass of the blastocyst becomes pluripotent. The source of pluripotent cells is this structure [8].

All germ layers' cells can be formed by pluripotent stem cells (PSCs), however extraembryonic tissues like the placenta cannot. Stem cells from embryos are one instance (ESCs). The inner cell mass of preimplantation embryos gives rise to ESCs. Utilizing implanted embryos' epiblast layer, induced pluripotent stem cells (iPSCs) can also be produced. Whereas multi-, oligo-, or unipotent cells have reduced potency, ESCs and iPSCs contain fully pluripotent cells [9]. The teratoma development assay is one way to evaluate their spectrum and activity. Pluripotent stem cells and artificially created pluripotent stem cells (iPSCs) have comparable functions. Their cultivation and use hold great promise for both current and future regenerative therapy [10].

A multipotent stem cell has a small differentiation spectrum than a PSC, but it can specialize in discrete cells of a specific lineage. An example would be a hematopoietic stem cell, which may grow into a variety of different types of blood cells. Hematopoietic stem cells differentiate into oligopotent cells after differentiation [11]. The differentiation ability of the cell is then restricted to cells of the same lineage [12]. However, some multipotent cells have the ability to differentiate into distinct cell types, indicating that they are in the

pluripotent category. Different types of cells can be differentiated from oligopotent stem cells. It is possible for myeloid stem cells to divide into white blood cells, but not into red blood cells [13].

Unipotent stem cells are characterized by limited differentiation capabilities and the ability to divide repeatedly. Considering their latter feature, they are promising therapeutic candidates for regenerative medicine. Cells of this type can only form one type of cell, e.g. dermatocytes [14].

### III. AN OVERVIEW OF CURRENT CLINICAL APPLICATIONS FOR STEM CELL-BASED THERAPY

- 1. Cardiovascular Diseases:** Recent reviews have discussed stem cell-based therapies for heart diseases in depth. In the following sections, hPSCs and MSCs will be discussed in light of these findings. Stem cell-based therapeutics in general, and adult stem cell therapy in particular (such MSC-infused products) are supported by preclinical and clinical trials [15]. Clinical trials have not yet shown the treatment's effectiveness because a number of research have yielded inconsistent results and have not discovered any statistically significant differences in infarct size, cardiac function, or clinical outcomes [16]. A meta-analysis revealed that there was no therapeutic benefit of stem cells from various sources on myocardial contractility, cardiovascular remodeling, or clinical outcomes [17]. Because the delivered cells could exert their therapeutic benefits through immunological regulation rather than regenerative action, clinical trials conducted thus far have yielded poor results [18]. Phase III trials that are carefully planned, randomized, and placebo-controlled, incorporating suitable patient selection, follow-up protocols, cell preparation techniques, and clinical assessments, are necessary to ascertain efficacy [19].
- 2. Digestive System Diseases:** Gastrointestinal disorders are among the most prevalent illnesses in the developed world, affecting one-third of the lives of Westerners [20]. A single layer of epithelial cells lining the gastrointestinal tract protects it from harmful compounds found in the gut environment. These cells are known to have an amazing capacity to regenerate themselves in response to injuries and normal cell turnover [21]. These epithelial cells divide every two to seven days in a normal state, and significantly faster in an inflammatory or damaged tissue. This rapid multiplication is made possible by the intestinal crypts' strong compartmentalization of stem cells [22]. The gastrointestinal system is extremely susceptible to illnesses, tissue inflammation, and injury as soon as the mucosal lining layer is compromised. When intestinal stem cells are exposed to their surroundings, the stem cell layer may be directly destroyed or digestion processes may be interfered with [23]. Extensive clinical signs could result from this. Furthermore, chronic inflammation, stress, and the accumulation of stem cell abnormalities all contribute to the decline in intestinal stem cell quality [24]. The two most common types of inflammatory bowel disease (IBD) in terms of digestive diseases are Crohn's disease (CD) and ulcerative colitis, both of which place a heavy strain on the healthcare system. The former is a long-term, uncontrollably inflammatory illness of the intestinal mucosa that manifests as granulomatous alterations and segmental transmural mucosal inflammation [25]. The latter is a persistent inflammatory bowel illness that affects the colon and rectum. It is characterized by mucosal inflammation that starts in the

rectum and continuously extends proximally to the colon. MSC-based therapy and hematopoietic stem cell-based therapy are the two categories of cellular therapy used to treat CD [26].

- 3. Liver Diseases:** The liver's many roles in the body include vitamin storage, metabolism, support for digestion, and detoxification [27]. It is the body's largest essential organ. Pathological disorders include liver failure, cirrhosis, cancer, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD), and autoimmune liver disease (ALD) can result from disruptions of liver homeostasis and function. Orthotropic liver transplantation is the only successful treatment for severe liver disorders, however there are very few donors who meet the requirements [28]. HSCs, MSCs, hPSCs, and liver progenitor cells are now linked to stem cell-based treatments for liver disease.
- 4. Nonalcoholic Fatty Liver Disease (NAFLD):** The most common medical condition is nonalcoholic fatty liver disease (NAFLD), which is brought on by both genetic and lifestyle factors [29]. It leads to severe liver damage and increases the risk of cardiovascular disease. Patients with NAFLD are often asymptomatic for long periods of time, and their everyday lives are unaffected. It is difficult to diagnose, identify, and treat NAFLD disorders because people with NAFLD frequently experience cirrhosis, hepatocellular carcinoma, and nonalcoholic steatohepatitis [30]. Few human clinical trials have been carried out, while preclinical research has demonstrated that stem cell injection can enhance liver function in NAFLD models [31]. Seven NAFLD patients were treated in a multi-institutional clinical trial conducted in Japan using recently identified autologous adipose tissue-derived regenerative cells. Six patients showed an improvement in serum albumin levels and five showed an improvement in prothrombin activity, and no serious adverse events were reported. NAFLD can be treated with stem cell-based therapy in this study [32].
- 5. Arthritis:** Inflammation and pain in the joints are symptoms of arthritis, a condition affecting cartilage. Osteoarthritis (OA), the most prevalent type of arthritis, is brought on by ongoing degradation and inadequate cartilage regeneration [33]. One or more diarthrodial joints, such as the big knee and hip joints and the tiny hand joints, are affected by OA, resulting in excruciating pain and limited range of motion. Primary OA is brought on by idiopathic factors, such as birth aberrant joint development, trauma, or surgery, while secondary OA is brought on by causal factors, such as the same [34]. A more dependable, less painful, and curative treatment for the underlying cause of OA is needed, as present treatments are not always effective and can cause severe pain and need long-term rehabilitation (in the case of joint replacement). Recently, stem cell therapy has gained a lot of attention in the field of regenerative medicine as an alternative treatment for osteoarthritis [35]. It has been demonstrated that HSCs improve bone regeneration, lessen bone lesions, and promote cartilage vascularization. Three intraarticular injections of peripheral blood stem cells were used to assess the effectiveness of the treatment in ten patients with osteoarthritis [36]. The WOMAC index decreased after injection, and all parameters significantly decreased as well, according to post-administration study. Every patient finished a 6-minute walk test with a gain of greater than 54 metres [37]. An improvement in cartilage thickness was seen in the MRI scan, indicating a decrease in cartilage deterioration following dosing. It was suggested that CD34+ stem cells be

employed in conjunction with the rehabilitation algorithm, which consisted of three stages: preoperative, hospitalisation, and outpatient periods, in order to further maximise the therapeutic potential of HSCT [38]. Because of their anti-inflammatory properties and immunoregulatory capabilities, MSC-based therapy has recently been the focus of a significant number of research for the treatment of osteoarthritis. MSCs have been the primary cell source in numerous small-scale and multiple experiments aimed at reducing cartilage degeneration, improving cartilage structure and morphological regeneration, and easing pain [39].

- 6. Cancer Treatment:** In cancer treatment, stem cell therapy is a responsive term that should be used and discussed with caution [40]. Patients should be shielded from the possibility of cancer as well as from the costly and potentially harmful stem cell therapies for those who do not have the disease. Three cell-based therapies, autologous hematopoietic stem cells (HSCTs), stromal vascular fraction (SVF), and multipotent stem cells (MSCs), were employed to treat cancer in the majority of untested stem cell clinics. "Graft-versus-tumor effects" refers to the ability of donor lymphocytes to suppress and inhibit solid tumours and haematological malignancies as a result of allogeneic HSCTs [41]. However, the safety and effectiveness of allogeneic cell-based therapy for solid tumours are not well supported by scientific research. According to Cochrane data, women with metastatic breast cancer do not have a better overall prognosis while receiving high-dose chemotherapy in addition to autologous HSCTs [42]. Moreover, there was no discernible difference between individuals who received HSCTs after high-dose chemotherapy and those who received conventional therapy in a trial including over 41,000 breast cancer patients [43]. Therefore, it is deemed false to promote autologous T-cell transplants as monotherapy and to portray stem cell-based therapies as medically recommended or approved treatments for solid tumours [44]. ClinicalTrials.gov currently lists 25 clinical trials testing MSCs as a cancer therapy. Most of these trials focus on evaluating the safety and efficacy of the treatment in phase 1 and 2. A combination of MSCs and oncolytic viruses has been studied in studies exploiting MSC-based therapy. Genetically engineered or naturally occurring viruses known as "oncolytic viruses" selectively infect and kill cancer cells without endangering nearby healthy cells [45]. A phase I/II study treating metastatic and refractory solid tumours in adults and children with BM-MSCs infected with the oncolytic adenovirus ICOVIR5 revealed that the treatment was safe and that some preliminary findings suggested its promise as a therapeutic [46]. In one pediatric case three years after MSC-based therapy was administered, all signs of cancer were completely gone. According to a study published in 2019, adipose-derived MSCs infected with vaccinia virus can eliminate resistant tumor cells through virus amplification and senescence [47]. With advancements in both stem cell-based therapies and more conventional medicines like radiotherapy, chemotherapy, and surgery, cancer research and therapy have entered a fascinating and new era. Although stem cell-based therapy is thought to be a unique and appealing therapeutic method, preclinical research have shown inconsistent results regarding its protumor and antitumor effects. Despite this paradoxical reality, cancer patients can benefit from a new and improved personalised medicine tool through stem cell-based therapy, particularly with MSCs. By inhibiting cancer cells' growth, eliminating cancer cells, or slowing the vascularization of malignant tissue, MSC-based therapy acts as a Trojan horse to deliver

particular anticancer properties to cancer cells, hence enhancing the treatment's efficacy and safety.

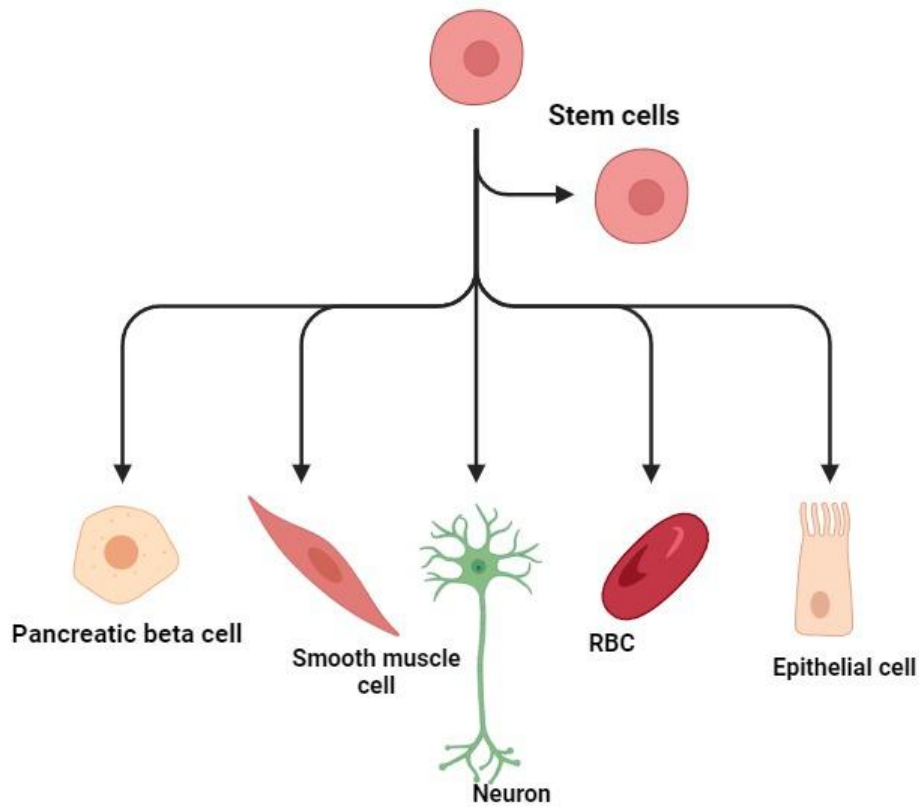
#### IV. CONCLUSION

Stem cell therapy is emerging as a tremendous medical game changer following several decades of research. Every experiment that is conducted shows that stem cells have more potential, yet many problems remain to be resolved. A interesting contemporary treatment option for a number of chronic and life-threatening diseases is stem cell therapy. All types of stem cells have enormous medicinal potential. Applications for stem cell therapy in medicine and dentistry are essentially endless. However, before this revolutionary therapy is brought from the lab to the clinic, a number of obstacles must be removed. Tissue engineering of teeth and tissues connected to teeth has become possible due to recent advancements in growth factor biology, biodegradable polymer structures, and stem cell isolation and expansion techniques. Researchers, physicians, and most importantly, patients who stand to gain the most from this breakthrough are filled with a great deal of hope and optimism because of stem cell therapy. Hope is renewed by stem cells.

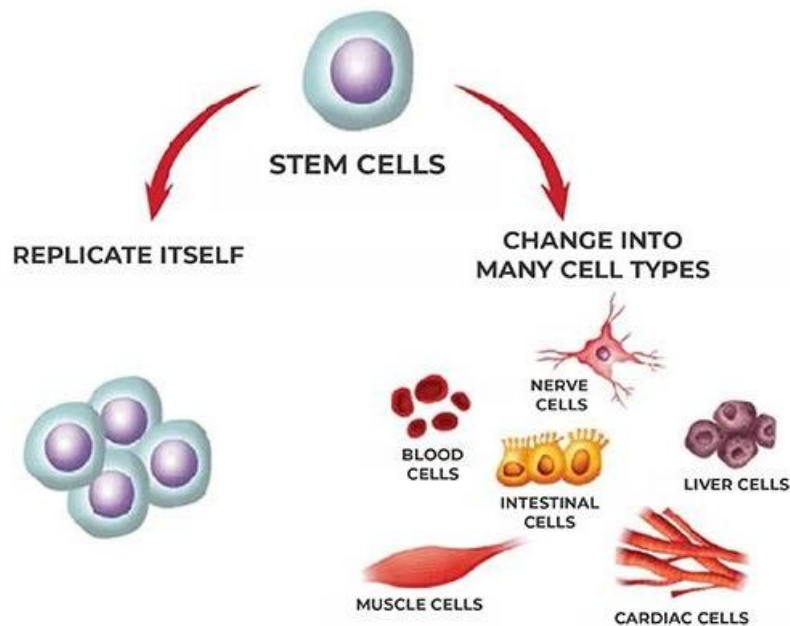
**Table 1: Advantages and Disadvantages of Stem cell**

Stem cells	Advantage	Disadvantages	Reference
NSCs	<ul style="list-style-type: none"> <li>➤ stem cell prototypes for the treatment of neurological disorders</li> <li>➤ It is possible to generate NSC-like cells from pluripotent and multipotent stem cell types.</li> </ul>	<ul style="list-style-type: none"> <li>➤ Restricted resource with ethical implications for purchasing</li> <li>➤ Inadequate comprehension of stem cell biology and minimal investigation in clinical trials</li> <li>➤ Risks of carcinogenesis if produced from pluripotent stem cells</li> </ul>	[48]
HSCs	<ul style="list-style-type: none"> <li>➤ An internationally recognised method of treating haematological disorders</li> <li>➤ An established enterprise for gathering and preparing treatments of clinical quality</li> </ul>	<ul style="list-style-type: none"> <li>➤ Restricted experience in treating neurological conditions</li> <li>➤ Generally restricted to use as an autologous therapy (if utilised as an allogeneic treatment, donor and recipient must match genetically)</li> <li>➤ Inadequately comprehended mechanism of action for managing specific neurological disorders</li> </ul>	[49]
MSCs	<ul style="list-style-type: none"> <li>➤ Easily obtained and readily available</li> </ul>	<ul style="list-style-type: none"> <li>➤ Used worldwide by unregistered clinics</li> </ul>	[50]

	<p>resource. Not required to match genetically</p> <ul style="list-style-type: none"><li>➤ It is highly probable that stem cell therapy will develop into a readily available allogenic product.</li></ul>	<ul style="list-style-type: none"><li>➤ Inadequately comprehended mechanism of action for managing specific neurological disorders</li></ul>	
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**Figure 1: Stem Cells and its Presence**



**Figure 2: Stem Cells and its Presence**

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