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Stem Cell Therapy, the Market, the Opportunities and the Threat

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ABSTRACT

Stem cell therapy is going to become the most widely used type of therapy in regenerative medicine. The stem cell therapy market has grown at an exponential rate in recent years. The purpose of the present paper is to review the stem cell market and the factors affecting it. The methods used included a literature review across reputable databases, and identifying articles and trusted financial reports related to the stem cell therapy market. Results show that the stem cell market growth rate is increasing, so that, the global stem cell market size was valued at US$297 million in 2022 and is anticipated to grow at a compound annual growth rate of 16.8% from 2022 to 2027, driven by factors such as clinical trials with promising results, increasing funding for stem cell research, growing number of technologies and facilities for cell therapy, and rising demand for regenerative medicine. However, the market also faces some challenges such as ethical concerns, regulatory hurdles, and the high cost of stem cell therapies and products. To enhance the development of the market further, policymakers and regulatory bodies must simplify the complicated process of obtaining regulatory approvals for clinical use. However, there are growing concerns about the increasing number of unapproved treatments using stem cells.

Keywords: Stem cells, market, therapies, clinical trials

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Introduction

Stem cell therapy is a certain type of regenerative medicine that deals with the process of transplanting human stem cells to restore or establish the normal function of tissues (1). Stem cell therapy is not a novel therapeutic medicine approach, as it encompasses bone marrow transplantation. Regarding the recent promising findings in regenerative medicine, stem cell therapy using hematopoietic stem cells (HSC), mesenchymal stem cells (MSC), and induced pluripotent stem cells (iPSC) have received much attention. Two major characteristics of stem cells that make them powerful tools for regenerative medicine are self-renewal and potency. Self-renewal is the ability to extensively proliferate, and potency refers to the ability to differentiate into various end cells. Different stem cells show some extent of difference in these properties. For example, among all kinds of stem cells, embryonic stem cells (ESCs) derived from the blastocyst show the greatest capability for self-renewal and potency. In contrast, adult stem cells have limited self-renewal and potency (2).

Stem cell therapy, usually, is comprised of a series of laboratory and clinical steps. At first, the stem cells are isolated from a donor (allograft) or own patient's (autograft) tissue. Then the isolated stem cells proliferate and differentiate in vitro using a culture medium and specific growth factors. In autograft circumstances, gene editing may be necessary to modify the genome of the patient's stem cells. Subsequently, the expanded stem cells or differentiated end cells are transplanted into the patient to regenerate the desired tissue cells (3).

Stem cell therapy is a multidimensional service that is provided by clinics, companies that provide equipment and materials for stem cell culture, insurance companies and other related services. In addition, regulatory bodies are directly engaged with all parts of the process, from research to translated applications. Data analysis shows that the stem cell market has been growing rapidly in recent years. Introduction the induced pluripotent stem cells by Yamanaka -a Nobel Prize laureate - fueled the growth rate of the stem cell market in the 2010s. In addition, technologies such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) have enhanced the growth rate of the stem cell market. In this paper, we summarized the latest progresses in the realm of stem cell therapy and took a glance at the size of the stem cell market. In addition, challenges that threaten the stem cell market growth rate has been discussed.

Methods

The primary objective of this narrative review is to analyze the current landscape of the stem cell therapy market, focusing on identifying opportunities and potential threats. The methodology encompasses a comprehensive literature search, analysis, and synthesis of relevant studies, reports, and market trends. A systematic search across reputable databases, including clinical trials.gov, Food and Drug Administration (FDA), European Medicines Agency (EMA), PubMed, and relevant academic journals, to identify articles, reviews, and reports on stem cell therapy market dynamics was conducted. A literature search of stem cells was performed using the keywords "stem cell clinical trials" and "stem cell market". Selected studies and reports provided insights into the stem cell therapy market, opportunities for growth, and potential threats. Publications that focus on market trends, regulatory landscape, technological advancements, and challenges associated with stem cell therapy were Included in the study.

Stem cell market

The clinical translation of stem cell knowledge is progressing rapidly to treat life-threatening disorders. The number of companies that provide services for regenerative medicine, including stem cell therapy, has increased globally from 772 in 2016 to over 1550 in 2024(4, 5). Over 8000 stem cell products clinical trials are ongoing or have been completed worldwide by the end of February 2023 (6). The global stem cells market grew at an incredible compound annual growth rate (CAGR) of 25.5% from 2015 to 2022 and reached a market value of US$297 billion by 2022 (7).

Several factors positively affect the growth rate of the market. The increasing demand for stem cell banking, expeditious raises in the aged population, the increment in governmental support, and rising research and development funding provided by the private sector are among the most important factors that will drive market growth. The researchers see the increasing number of stem cell banks, the rising focus on the growing therapeutic potential of stem cell therapies, and extensive research to develop regenerative medicines" as indicators of the growing market. The introduction of iPSC as an alternative to ESC, and the rapid progress of novel stem cell therapies, predict growth opportunities for investors in the market (7). According to reports, the global stem cell market will reach $558 million by 2027 (8). In addition, it is expected that increased governmental support for cancer research and the progress of stem cell therapies to treat malignancies influence the stem cell market growth rate positively(9).

Currently, the stem cell therapy market is segmented into a larger part i.e., allogeneic stem cell therapy, and a smaller part i.e., autologous stem cell therapy. It seems that higher opportunities in the stem cell therapy market will arise in the allogeneic stem cell therapy segment in the next few years. The use of autologous cells is expected to decrease from 56% to 35% by 2029 (10). One reason is the high cost of preparation and treatment for only one patient (10). Therefore, investing in allogeneic stem cell therapy is more valuable.

In addition, according to the stem cell source, the market is divided into several parts including adult stem cells, iPSCs, and ESCs. The adult stem cells segment is the largest part of the stem cell market now. Going forward, the iPSCs segment is expected to be the fastest growing segment in the stem cell therapy market, at a CAGR of 9.5% during 2022-2030 (11). Currently, in terms of the type of stem cells, the most profitable sector is related to adult stem cells such as HSC, MSC then iPSC (12). According to predictions made regarding MSC and iPSC, investment in this field will be very profitable (13).

As well, according to the disorders, the stem cell therapy market and their related research are divided into the treatment of hematologic disorders, wounds, burns and cosmetics therapies, cancer therapy, and autoimmune disorders treatment. Up to now, the hematologic disorders segment has been the largest segment of the stem cell therapy market, accounting for 49.7% of the total in 2022(14). During the past 50 years, more than 1 million HSC transplants have been done in patients with hematological malignancies(15). Such therapies are routinely used to treat leukemia, aplastic anemia, thalassemia, sickle cell anemia, and heritable metabolic disorders. The analysis showed that the size of the bone marrow transplantation market was at $10.35 million in 2022 and is forecasted it grows at a CAGR of 3.7% from 2022 to 2028, and reach $12.8 million by 2028 (16). It is estimated that the cost per stem cell treatment is between US$10 000 and US$60 000 (17). Going forward, the treatment of autoimmune diseases such as diabetes as well as wounds,

burns, and cosmetics segments is expected to be the fastest growing segment in the stem cell therapy markets, at a CAGR of 22.1% during 2021-2026 Figure 1 (8).

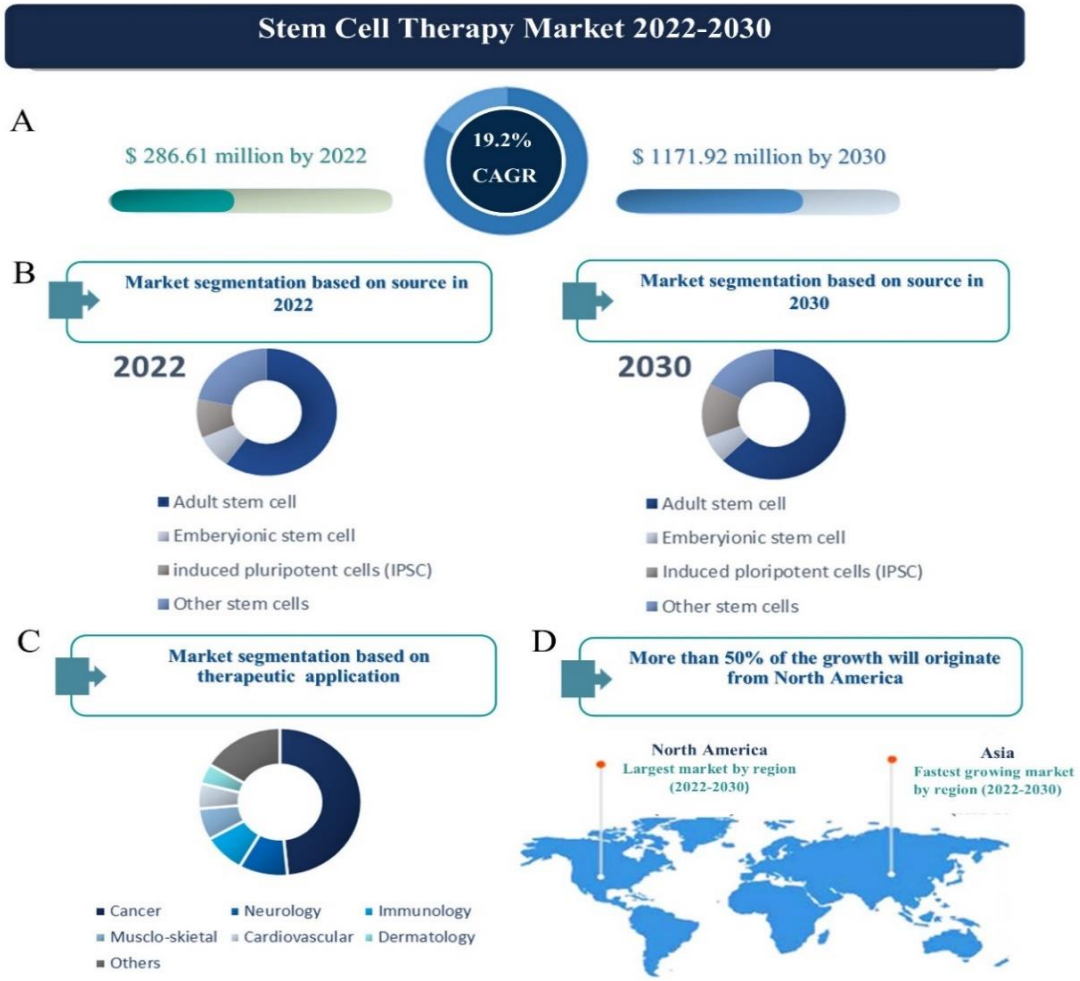

Fig. 1. Stem cell therapy market. (A) The global stem cell market size was valued at US$286.61 million in 2022 and is expected to reach US$1,171.92 million in 2030. It is expected to grow at a compound annual growth rate of 19.2% from 2022 to 2030. The stem cell market is segmented based on sources, therapeutic applications, and regions. (B) By source, the market is classified into adult stem cells, embryonic stem cells, induced pluripotent stem cells (iPSCs), and other cell sources. (C) The market is classified into several divisions regarding therapeutic applications, including cancers, musculoskeletal disorders, wounds and injuries, cardiovascular diseases, neurological disorders, and other diseases. Stem cell-based cancer treatments have the major revenue, and it is expected to continue this trend during the forecast period. (D) Geographically It is classified into North America, Europe, Asia-Pacific, Middle-East and Africa, and South America. North America is expected to have the highest stem cell therapy market growth rate.

Looking at the stem cell market based on the region reveals that by 2021 North America, Western Europe, and Asia Pacific share the most. Among them, the North American region had more than 50% of the share. The United States is a major player in markets of stem cell banking and clinical services, which accounts for about 77.4% of the entire North American market. However, Asia-Pacific is growing at the

highest growth rate (7). Although the analysis shows that the playground will be changed in near future. Now, South America and the Middle East have the fastest-growing rate, Eastern Europe and the Asia Pacific will follow them (8). The markets are developing owing to the increase in R&D investments and ease of regulations related to stem cell investigation and therapy. The changing lifestyles have increased the incidences of chronic diseases. Furthermore, clinical trials using stem cell therapies and introducing new and innovative technologies for utilizing stem cell therapies enhance the market growth (18, 19). Therefore, governments and policymakers are under pressure to facilitate investments in regenerative medicine (7). In the following, we review some clinical trials and milestone technologies that could positively affect the market of stem cell therapy.

Clinical trials as a driving force for the stem cell market

In recent years numerous researches including clinical trials focused on the stem cells realm. The data obtained from three clinical trial databases (ClinicalTrials.gov, the International Clinical Trials Registry Platform (ICTRP) of the World Health Organization, and the European Union Drug Regulating Authorities Clinical Trials (EudraCT)) showed that 1199 clinical trials of stem cells have been performed between 1999 and Feb 2023. These studies cover a wide range of diseases and conditions, such as cancer, cardiovascular diseases, neurological disorders, autoimmune diseases, diabetes, spinal cord injury, and more. Some of the studies are phase 1 or phase 2 trials that aim to test the safety and feasibility of stem cell therapy, while others are phase 3 or phase 4 trials that aim to test the efficacy and compare the outcomes with other treatments. A glance looks at the data reveals that so far, North America, especially the United States, conducted most of the approved clinical trials based on stem cell therapy. Despite the substantial number of clinical trial studies conducted on stem cell therapy and their promising results (20, 21), up to now a few products for clinical uses are approved by regulatory agencies (22, 23). One main reason is that most of the evidence that was submitted to receive the biological licenses was obtained from studies that were sub-optimally designed and were likely to result in biased and imprecise conclusions. Indeed, the expected level of evidence for regulatory judgment is randomized double-blind placebo-controlled trials while the performed studies included small, single-arm, short-term, early-phase clinical trials. However, it's essential to highlight that the adoption of these study designs is not a choice, but rather is a result of the conditions associated with the patients undergoing stem cell therapies. Conducting clinical trials with two arms would require much time, and receiving great grants, because the population of patients with rare or severe diseases may be small. In addition, in situations where there is no alternative treatment, randomization to a control group is not ethically acceptable (24).

It is necessary to mention some clinical trials here. One of the most advanced fields of stem cell therapy is ophthalmology, where several trials have shown positive outcomes for patients with eye diseases such as age-related macular degeneration (AMD), corneal dystrophy, and retinitis pigmentosa. For example, in a clinical trial in Japan, iPSCs were differentiated into corneal cells and used (25). Another trial in China showed that injecting retinal pigment epithelial cells derived from human embryonic stem cells (ESCs), into the eyes of patients with AMD improved their visual acuity and reduced their central scotoma (26).

Another promising area of stem cell therapy is neurology, where several trials have explored the potential of stem cells to treat neurological disorders such as amyotrophic lateral sclerosis (ALS), spinal

cord injury (SCI), and stroke. For example, a trial in the USA reported that injecting fetal neural stem cells into the spinal cord of patients with ALS ameliorates disease progression(27). Another trial in South Korea showed that transplanting MSCs into the spinal cord of patients with SCI improved their motor and sensory functions and reduced pain (28). The results of a clinical trial in Germany demonstrated that infusing stem cells into the brain of patients with stroke enhanced their recovery and increased brain perfusion (29).

These are just some examples of the exciting results that stem cell therapy has achieved in clinical trials (Table 1). However, there are still many challenges and limitations that need to be overcome before stem cell therapy can become a routine clinical option for patients. Some of these challenges include ensuring the safety and efficacy of stem cell products, avoiding immune rejection and ethical controversies, optimizing the delivery and integration of stem cells, and scaling up the production and distribution of stem cell products. Therefore, more research and development are needed to advance the field of stem cell therapy and to translate its potential into clinical reality.

Table 1. The increase in clinical trials related to stem cell therapies over the past few years is expected to enhance the stem cell market growth rate. There are many clinical trials of stem cell therapy in several diseases, some of which are extracted from clinicaltrial.gov.

NCT number	Derived from	Clinical trial phase	Application	Sponsor country
NCT 03279081	Adult allogeneic expanded adipose	III	Treatment of complex perianal fistula(s) in patients with Crohn's disease	United States
NCT 04194671	Mesenchymal Stem Cells	I / II	Treatment of Severe Acute Kidney Injury	China
NCT 03225651	Autologous Bone Marrow Stem Cell	II	Treatment of Autism	Vietnam
NCT 04356287	Human Umbilical Cord-derived Mesenchymal Stromal Cells	I / II	Treatment of Systemic Sclerosis	Canada
NCT 03549299	Allogeneic ABCB5-positive Limbal Stem Cells	I / II	Treatment of Limbal Stem Cell Deficiency (LSCD)	United States
NCT 04553159	Autologous Adipose-Derived Stem Cells	II	Treatment of Keloids (Keloids are the most common disfiguring skin disorder affecting the colored population)	Uganda
NCT 02338271	Autologous Adipose Derived Stem Cell	I	Intervertebral Disc Degeneration	Korea
NCT 03361631	Autologous Mesenchymal Stem Cells	I	Treatment of Erectile Dysfunction Resistant to Oral Treatment in Patients with Type I Diabetes	France
NCT 04464213	Human Placental Mesenchymal Stem Cells	I	Treatment of Diabetic Foot Ulcer	China
NCT 03005249	Neural Stem Cells	Not Applicable	Cerebral palsy	China
NCT 04713878	Mesenchymal Stem Cells	Not Applicable	Patients with COVID-19 Pneumonia	Turkey

NCT 02675556	Allogeneic Human Mesenchymal Stem Cells	Ⅰ	Use for Treatment Resistant Depression (ANU)	United states
NCT 06145711	hiPSCs Derived Dopaminergic Neural Precursor Cells	Not Applicable	Treatment of Parkinson's Disease	China
NCT 02298023	Allogenic Adipose-derived Mesenchymal Stem Cells	Ⅱ	Treatment of Tendon Injury	Korea
NCT 00984178	Hematopoietic Stem Cells	Ⅱ	Treatment of Acute Myocardial Infarction	Spain
NCT 01809769	Autologous Adipose Tissue-Derived Mesenchymal Stem Cells	Ⅰ / Ⅱa	Treatment of Knee Osteoarthritis	China
NCT 01730547	Mesenchymal Stem Cells	Ⅰ / Ⅱ	Treatment of Multiple Sclerosis	Sweden
NCT 03167203	Human Embryonic Stem Cell-derived Retinal Pigment Epithelial Cell	Ⅰ / Ⅱ	Treatment of Macular Degenerative Disease	United States

NCT number: National Clinical Trial number. NCT is an identification that ClinicalTrials.gov assigns a study when it is registered.

Technology as a key factor for the growth of the stem cell market

Discoveries and progresses in the realm of stem cells have boosted their applications for therapeutic purposes. In this regard, many sophisticate techniques such as single-cell laser capture, microdissection, cell-sorting devices, and etc. have been used for stem cell isolation (30). In addition, various multidisciplinary technologies including CRISPR/Cas, microfluidic, three dimensions tissue culture, and tissue printing systems have been applied. However, stem cell therapy needs to overcome two manufacturing challenges: achieving standardized fully automated cell or tissue production methods and scaling up the technology to achieve final products vastly greater than the present level. In this regard, recently a biotechnology company (Essent Biologics™) has introduced the first commercially highly characterized, low-passaged human MSCs (31). Each vial contains over one million cells (P0 or P1 passage) which are expanded and cryopreserved without using antibiotics or animal products under the GMP standards. Moreover, a robust, fully automated culture system of adult stem cells is essential to commercialize tissue engraftment.

Recently, the world's first automated instrument to generate human skin tissue grafts from stem cells for severe skin injuries has been introduced by CUTISS (32). In addition, several encouraging milestones have been made by pioneer companies. For example, a self-organized aggregates technology was developed to produce a batch of 15 billion iPSCs in a week in the bioreactors (33). Likewise, a high-throughput platform that uses plasmonic intracellular delivery technology is introduced that may be suitable to fabricate autologous iPSCs. The platform is built by merging stem cell science, laser physics, and artificial intelligence (34, 35). The platform is composed of a culture vessel that is layered by a nano-structured absorbent membrane. When the membrane is stimulated by a laser beam, generates micro-bubbles that can permeabilize the plasma membrane of target cells to deliver molecular cargo to induce pluripotency.

Limitations and challenges of the regulations of stem cell therapies

The stem cell market and new technologies offer tremendous opportunities for innovation and improvement in human health. However, as technologies that are related to the domain of stem cells are largely in their infancy era, there are significant hurdles to translating stem cell technology from the bench to the bedside. According to the opinions of experts and stakeholders, in the near future, the most significant factors hindering the progress of the market are the overpriced stem cell therapy and the stringent requirements needed for obtaining a biological license set by regulatory bodies. With the advent of new stem cell therapies and to assure their appropriate quality, safety, and efficacy, any stem cell therapy should be approved by national or regional regulatory authorities. The regulations are diverse in different parts of the world. Some countries approved certain stem cell products and therapies that are not approved in other countries. Roughly speaking, regulatory bodies in the USA and the EU act more strictly than those in Japan and Australia (36). Despite this, there are growing concerns about the increasing number of non-approved therapies using stem cells. Employing stem cell therapies that have not been supported by scientific evidence menace legitimate research efforts to develop safe and effective therapies for patients whose diseases currently have no effective treatment (36, 37).

Conclusion

Stem cell therapy has great potential to induce a paradigm shift from supportive conventional therapy into definitive treatment. The stem cell market grew rapidly in recent years, and considerable investments have been made. In addition, the increasing number of clinical trials with promising results and approval of stem cell-based therapies make many opportunities for this market. However, stem cell therapy is still an emerging technology, therefore, in line with the Declaration of Helsinki (38) its clinical applications should be limited till its safety and efficacy be established. In addition, besides developing technologies to commercialize stem cell therapy, there is an urgent need to define regulations and rules to support healthcare systems to assume the cost of the development of stem cell therapy for a myriad of rare diseases and more common diseases of epidemic proportions.

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Conflict of interest

The authors declare that there is no conflict of interest related to this article.

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