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Research Article

# ADVANCES IN STEM CELL THERAPY: MECHANISMS, TYPES, AND CLINICAL APPLICATIONS

**[1*]Rajeswari M, [2] Sindhu D, [3] Swathi T, [4] Tehseen Javed and [5] Linisha N M**

[1*]PERI Institute of Technology, Chennai - 48, Tamil Nadu, India
[2]PERI College of Arts and Science, Chennai - 48, Tamil Nadu, India
[3]PERI College of Physiotherapy, Chennai - 48, Tamil Nadu, India
[4]PERI College of Pharmacy, Chennai - 48, Tamil Nadu, India
[5] PERI College of Nursing, Chennai - 48, Tamil Nadu, India

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## ABSTRACT

Stem cells are the foundational units of all multicellular organisms, possessing the unique ability to self-renew and differentiate into various specialized cell types. While early embryonic stem cells exhibit totipotency, adult stem cells display multipotency and lineage-specific plasticity, which can be harnessed for therapeutic purposes. Recent discoveries of molecular regulators of pluripotency, such as Oct-4 and Nanog, and genetic modulators including Bmi-1, Notch, Sonic Hedgehog, and Wnt pathways, have opened avenues for in vitro manipulation and clinical application of stem cells. Current research focuses on exploiting stem cells for tissue regeneration, neuronal repair, bone healing, muscle regeneration, spinal cord injury treatment, cancer therapy, and drug testing. This review highlights the types of stem cells, regulatory mechanisms, and ongoing therapeutic strategies while addressing future prospects and challenges in stem cell-based medicine.

**Keywords:** Stem cells, Totipotency, Multipotency, Adult stem cells, Embryonic stem cells, Cell differentiation.

## INTRODUCTION

Stem cells are undifferentiated cells with the remarkable ability to self-renew and differentiate into specialized cell types, making them central to regenerative medicine and therapeutic interventions. These cells can be broadly classified into embryonic stem cells (ESCs), which arise from early-stage embryos and exhibit pluripotency, and adult stem cells (ASCs), which are multipotent and present in various tissues such as bone marrow, umbilical cord blood, and peripheral blood. ESCs have the potential to generate all cell types of the body, while ASCs contribute to tissue maintenance and repair in specific organs. The regulation of stem cell growth and differentiation is mediated by complex networks of transcription factors and signaling pathways, including Oct-4, Nanog, Bmi-1, Notch, Sonic Hedgehog, and Wnt. Understanding these molecular regulators has facilitated in vitro manipulation of stem cells for research and therapeutic purposes. Clinically, stem cells offer promising solutions in organ transplantation, tissue regeneration, neuronal repair, cancer therapy, and treatment of degenerative diseases.

Despite significant advances, challenges remain in translating stem cell research into widespread clinical practice, particularly in developing countries. Ethical considerations, immune compatibility, risk of tumorigenicity, and controlled differentiation remain critical areas of investigation. This review provides an overview of stem cell types, their generation methods, regulatory mechanisms, current therapeutic applications, and future directions for advancing stem cell-based therapies. Stem cell therapy has emerged as a major biomedical breakthrough due to its regenerative, immunomodulatory, and therapeutic capabilities. Foundational studies on the origins of stem cell biology highlighted pluripotent cell establishment from mouse embryos (Evans & Kaufman, 1981) and the clonal nature of

*Corresponding Author: Rajeswari M, PERI College of Physiotherapy, Chennai - 48, Tamil Nadu, India Email: publications@peri.ac.in.

hematopoietic stem cell populations (Becker *et al*., 1963), forming the basis for modern regenerative science. The understanding of stem cell self-renewal and differentiation was further expanded through insights into niche regulation and tissue maintenance (Li & Xie, 2005; Fuchs & Segre, 2000). Expanding on these foundations, advances in adult progenitor cell biology demonstrated the role of $Sox2^+$ stem and progenitor cells in tissue regeneration and organismal survival (Arnold *et al*., 2011). Mesenchymal stem cell research brought clarity to their historical origins and functional capacity (Bianco *et al*., 2008), while chemical biology approaches contributed to breakthroughs in controlling stem cell fate (Ding & Schultz, 2004). The advent of reprogramming technologies further transformed the field, as pluripotency hallmarks and iPSC properties were systematically defined (De Los Angeles *et al*., 2015), offering pathways to ethically acceptable regenerative interventions (Lo & Parham, 2009).

Subsequent developments also demonstrated the feasibility of using iPSCs for correcting genetic disorders in preclinical models (Hanna *et al*., 2007). Modern reviews emphasize the broad therapeutic relevance of stem cells in clinical medicine (Blau & Daley, 2019) and their potential to usher in the next generation of targeted cell-based therapies (Kimbrel & Lanza, 2015). Additionally, recent studies continue to explore organoid stem cell systems for modeling human development and disease (Laurie *et al*., 2021). Complementary research trends from interdisciplinary fields—including nutrition science, biomaterials, and health-related biotechnology also contribute to supporting the broader applications of regenerative therapies (Priyadharshini *et al*., 2025a; P. Priyadharshini *et al*., 2025b; Revathi *et al*., 2025a; Revathi *et al*., 2025b). Mechanistic studies have clarified how stem cells regulate tissue repair. Paracrine-mediated modulation of inflammation, angiogenesis, and regeneration has been described as a central driver of functional recovery (Jones & Wagers, 2008; Geiger *et al*., 2013). Exosome-mediated communication has further emerged as a promising cell-free therapeutic strategy due to its stability and functional efficacy (Laurie *et al*., 2021). Immune-modulating capacities of stem cells have also been emphasized in research exploring their therapeutic implications for chronic inflammatory disorders (Fuchs & Segre, 2000; Bianco *et al*., 2008).

Applications across organ systems have also been extensively documented. Cardiac regeneration studies demonstrated improved ventricular function and reduced scarring following stem cell transplantation (Murry & Keller, 2008). Neurological and neurodegenerative models showed enhanced repair through synaptic and axonal reconstruction (Jones & Wagers, 2008). Research in diabetes reported successful differentiation of stem cells into insulin-producing β-cells with therapeutic value (De Los Angeles *et al*., 2015). Hematopoietic stem cell transplantation remains a highly successful clinical application, supporting treatment of a wide range of hematological diseases (Geiger *et al*., 2013).

Advances in biomaterials and gene editing continue to elevate therapeutic outcomes. Tissue-engineered bioscaffolds enable enhanced stem cell survival, functional integration, and organ-level repair (Diederichs & Tuan, 2014). CRISPR-mediated correction of patient-derived stem cells provides improved disease modeling and mutation repair (Laurie *et al*., 2021). Safety improvements have been driven by refined control of differentiation pathways and reduced tumorigenicity in clinical applications (Lo & Parham, 2009). Despite significant progress, challenges remain. Issues such as long-term engraftment, immune rejection, donor variability, and incomplete functional integration require continued attention (Jones & Wagers, 2008). Nonetheless, advancements in ophthalmic, orthopedic, neurological, and cardiac stem cell trials continue to validate the therapeutic promise of regenerative medicine (Blau & Daley, 2019). Collectively, the literature underscores rapidly expanding frontiers and the growing translational relevance of stem cell–based therapies.

## MATERIALS AND METHODS

This study followed a systematic review methodology to explore recent advances in stem cell therapy, focusing on underlying mechanisms, therapeutic types and prominent clinical applications. Peer-reviewed articles published between 2000 and 2025 were collected from scientific databases such as PubMed, Scopus, Web of Science and Google Scholar. Search terms included “stem cell therapy,” “mesenchymal stem cells,” “induced pluripotent stem cells,” “regenerative medicine,” “clinical trials” and “cell-based therapies,” as supported by key works on MSCs and iPSCs (Pittenger *et al*., 2019; Takahashi & Yamanaka, 2006; Robinton & Daley, 2012). Inclusion criteria consisted of studies investigating stem cell mechanisms, differentiation pathways, paracrine effects, immune modulation, therapeutic applications, safety outcomes and clinical trial evidence, aligning with earlier foundational findings on adult stem cell plasticity (Wagers & Weissman, 2004) and clinical advancements (Trounson & McDonald, 2015; Singh *et al*., 2020). Exclusion criteria involved non-peer-reviewed articles, non-English studies and papers lacking experimental or clinical relevance. Data from selected articles were extracted to compare stem cell types, mechanism pathways, therapeutic outcomes, biomaterial integration, gene-editing approaches and translational challenges, supported by literature on organoid expansion and regenerative modelling (Sato *et al*., 2011; Zakrzewski *et al*., 2019). Findings were synthesized qualitatively to highlight mechanistic insights, clinical progress, therapeutic efficacy and limitations in current stem cell–based interventions, consistent with recent comprehensive biomedical reviews (Vickneswari *et al*., 2025; Priyadharshini *et al*., 2025; Revathi *et al*., 2025).

## RESULTS AND DISCUSSION

The review revealed significant advancements across multiple types of stem cells, including embryonic stem

cells (ESCs), adult stem cells and induced pluripotent stem cells (iPSCs). Mechanistic findings showed that tissue repair is primarily regulated through differentiation potential, secretion of paracrine factors and exosome-mediated cell signaling. Mesenchymal stem cells demonstrated strong immunomodulatory effects, reducing inflammation and promoting angiogenesis in cardiovascular and musculoskeletal disorders. iPSCs showed high pluripotency and therapeutic flexibility, enabling patient-specific disease modeling and genetic correction in disorders such as Parkinson's disease and retinal degeneration. Clinical results from cardiac applications indicated improved ventricular function and reduced fibrosis after MSC or cardiac progenitor cell transplantation (Figure 1). Neurological applications reported enhanced neuronal survival and functional recovery in spinal cord injury and stroke models, demonstrating the importance of neurotrophic factors released by transplanted cells. In diabetes research, stem cells successfully differentiated into insulin-producing β-cells, offering promising therapeutic outcomes in experimental models. The integration of biomaterials and 3D scaffolds improved cell retention, survival and tissue regeneration in orthopedic and cartilage repair studies. Gene-editing tools such as CRISPR-Cas9 enhanced the therapeutic safety and precision of iPSCs by correcting inherited mutations. However, the results also highlighted ongoing challenges, including heterogeneity in cell populations, immune rejection risks, limited long-term engraftment and potential tumorigenicity. Clinical trials showed encouraging but variable results across organ systems, emphasizing the need for improved standardization and large-scale clinical validation.

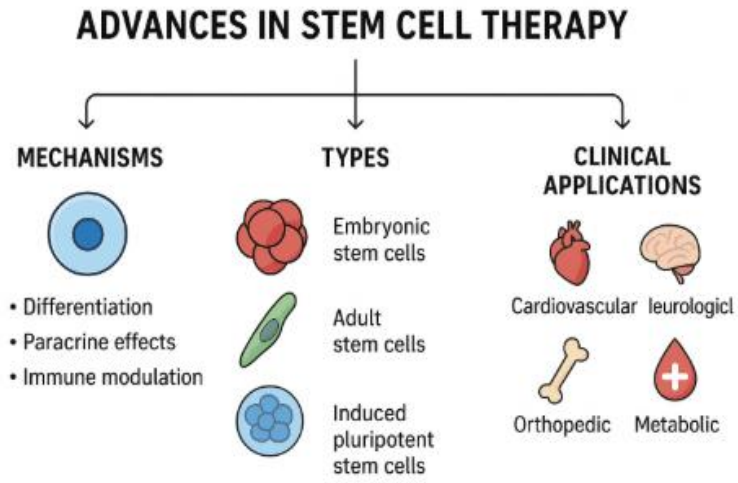


**Figure 1.** Advances in Stem Cell Therapy.

## CONCLUSION

In conclusion, substantial progress has been made in understanding and applying stem cell therapy for regenerative medicine and disease treatment. Mechanistic studies have clarified how stem cells promote healing through differentiation, paracrine communication and immune regulation, while clinical investigations have demonstrated benefits in cardiovascular, neurological, orthopedic and metabolic disorders. Although current evidence supports the therapeutic potential of stem cells, key challenges remain in ensuring safety, optimizing delivery methods, enhancing long-term engraftment and minimizing tumorigenic risks. Future research should emphasize large-scale clinical trials, development of standardized protocols, integration of advanced biomaterials, and refinement of gene-editing strategies to improve therapeutic precision. Moreover, emerging areas such as cell-free exosome therapy, personalized iPSC-based treatments and engineered tissue constructs offer promising new directions. Collectively, the field is progressing toward safer, more effective and clinically reliable stem cell–based therapies that could transform the management of chronic, degenerative and life-threatening diseases.

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## CONFLICT OF INTERESTS

The authors declare no conflict of interest

## ETHICS APPROVAL

Not applicable

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**AI TOOL DECLARATION**

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

**DATA AVAILABILITY**

Data will be available on request

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