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FROM GENOMES TO REGENERATIVE THERAPEUTICS: INTEGRATING OMICS, STEM CELL SCIENCE, AND PRECISION MEDICINE IN LOW- AND MIDDLE-INCOME COUNTRIES

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Abstract

Regenerative medicine is rapidly evolving toward a precision-based discipline in which therapeutic strategies are tailored to each patient's molecular and genomic profile. At the center of this transformation are stem cells, whose regenerative and immunomodulatory properties, combined with advances in precision medicine, are redefining approaches to the treatment of complex diseases. The integration of multi-omics technologies including genomics, transcriptomics, proteomics, metabolomics, and epigenomics with artificial intelligence (AI) has expanded our understanding of stem cell biology, enabling more accurate biomarker discovery, improved patient stratification, and the rational design of personalized regenerative therapies. Recent technological advances have further accelerated progress in this field. Genome engineering approaches such as CRISPR, base editing, and prime editing, together with gene therapy, synthetic biology, organoid technology, extracellular vesicles, cell-free therapeutics, 3D bioprinting, digital twins, and organ-on-chip platforms, are reshaping both experimental research and clinical translation. Collectively, these innovations are improving the precision, safety, and therapeutic potential of stem cell-based interventions. This review provides a comprehensive overview of the molecular characteristics of stem cells, the role of multi-omics and AI in precision regenerative medicine, and the emerging technologies driving next-generation regenerative therapeutics. It further examines current and potential applications of stem cell–based therapies across a broad spectrum of diseases, including cancer, neurological, cardiovascular, metabolic, musculoskeletal, autoimmune, ocular, and rare genetic disorders. Particular attention is given to the opportunities and challenges facing low- and middle-income countries (LMICs), where limitations in infrastructure, funding, regulatory capacity, manufacturing, and skilled workforce continue to restrict clinical implementation despite growing research activity. By integrating recent advances in stem cell biology, precision medicine, immunology, and translational biotechnology, this review presents a comprehensive perspective on the current state of regenerative medicine while highlighting the scientific, clinical, and policy

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priorities needed to advance safe, effective, and equitable stem cell therapies worldwide.

Introduction:

1.1 The Evolution of Regenerative Medicine

The classic idea of treating a disease has evolved. Now, the focus is on restoring damaged tissue and the associated organ's function, rather than just managing symptoms. To repair, replace, or regenerate damaged cells and tissues, regenerative medicine brings together stem cells, biomaterials, tissue engineering, and sophisticated biotechnological approaches. Consequently, new treatment prospects have been created for diseases that were previously hard, if not impossible, to treat, including chronic, degenerative, or inherited conditions(McKinley et al., 2023; Rasekh et al., 2025).

Clinically, it was the successful administration of hematopoietic stem cell transplantation that provided proof of concept for regenerative medicine, establishing that stem cells could effectively restore tissue function and promote tissue regeneration(Lee & Hong, 2020). The isolation of human embryonic stem cells in 1998 and the development of induced pluripotent stem cells (iPSCs) in 2006 were major milestones in the history of the regenerative medicine field that made it possible to obtain renewable sources of pluripotent stem cells for applications in regenerative medicine, disease modelling, drug discovery and development, toxicity testing, and personalized treatment(Liu et al., 2020).

The fast-paced development of molecular biology and high-throughput technologies has further supported the growth of regenerative medicine. The rapid progress in genomics, transcriptomics, proteomics, and epigenomics has helped us better understand the molecular processes involved in stem cell self-renewal and differentiation as well as in tissue regeneration (Ma et al., 2024). Likewise, the emergence of genome editing techniques using CRISPR and associated tools, the development of single-cell sequencing approaches, organoid technologies, tissue engineering, and three-dimensional (3D) bioprinting technology has opened up the possibility for the creation of precision regenerative therapies customized to individual patients (Rasool et al., 2026). This progress has also led to the adoption of the precision medicine principle in which each patient's genetic makeup, molecular properties, clinical course of illness, and exposure to environmental elements is considered as a whole for the purpose of selecting therapeutic strategies and improving disease outcomes. Thus, the use of stem cell biology in the context of multi-omics technologies and the application of precision medicine have led to the concept of precision regenerative medicine, which refers to tailoring regenerative therapy based on the individual patient characteristics. By applying this patient-specific approach, it has been hoped that therapeutic efficiency could be maximized and adverse events minimized (Zayed et al., 2026).

Despite these advances in regenerative medicine, the benefit derived from the treatment has been unevenly distributed globally. The developed world has seen the rapid progress of stem cell-based regenerative medicine owing to its commitment to investing in research, establishing regulatory frameworks, enhancing production capacity, and translating basic scientific discoveries into clinical practice, all of which have contributed to improved translation of stem cell-based regenerative medicine(Marchal, 2025). On the other hand, many low- and middle-income countries (LMICs) have been unable to take full advantage of recent scientific and clinical advances in stem cell-based therapy because of their limited resources in areas such as funding, laboratory infrastructure, training for scientific human resources, and capacity for accessing cutting-edge genomic and genomic-related techniques (Boakye Serebour et al., 2024). The efforts to ensure equity will be important so that the fruits of advances in regenerative medicine reach more patients worldwide.

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1.2 Stem Cells as the Foundation of Precision Therapeutics

Stem cells are the foundation of regenerative medicine because they can regenerate themselves and differentiate into different types of cells. Therefore, stem cells can be used to replace cells or tissues that have been damaged, to repair cells or tissues, or to restore normal function of cells or organs in a wide variety of disease states (Casado-Díaz, 2022). As a result of these features, they are widely considered to have promising clinical prospects in regenerative treatments, and the ultimate aim of stem cell-based treatment is to cure the causes of disease and injury rather than treating the symptom(Casado-Díaz, 2022).

Currently, five principal categories of stem cells have been described: embryonic stem cells (ESCs), adult stem cells, mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs) and perinatal stem cells. In the context of precision medicine, iPSCs provide a useful approach because they are derived from a person's own tissues, therefore are less likely to cause an immune response, or ethical controversy. MSCs have also gained attention because of their regenerative, immunomodulatory and anti-inflammatory properties, and are considered promising therapy for the treatment of autoimmune diseases, musculoskeletal, cardiovascular and inflammatory diseases (Aboul-Soud et al., 2021).

In recent years, with the increasing focus on the concept of precision medicine and personalized treatment, the use of stem cells in regenerative therapies to fit each patient's unique needs, is gaining increasing attention. Because the concept of precision medicine emphasizes on an individual's genetic variation, environmental factors, lifestyle habits and molecular features, combining these elements will allow the development of stem cell-based regenerative treatments customized to the specific profile of each patient (Yildirim et al., 2025). For instance, iPSCs derived from a patient can be a platform for modeling disease, drug testing, identifying the toxicity, development of individualized therapies and other research projects in clinical precision(Aboul-Soud et al., 2021).

In recent years, multi-omics technologies, including genomics, transcriptomics, proteomics and epigenomics, have provided new insights into the molecular pathways regulating stem cells and their involvement in tissue maintenance and regeneration(Ma et al., 2024). These technologies can be used to identify biomarkers of disease progression or prognosis, therapeutic targets and molecular pathways that could be altered or targeted. In addition, new and improved genome editing platforms, such as CRISPR-Cas systems, can be used to correct the genetic variants that cause diseases before stem cells are used for treatments, which can improve the safety and precision of the procedure(Rasool et al., 2026).

Although advances in these technologies have made them widely used in high-income countries, implementing these therapies is difficult for low- and middle-income countries because access to sophisticated equipment such as next generation sequencing technology and advanced laboratory platforms and facilities, manufacturing technologies, infrastructure and regulatory systems (Doxzen et al., 2024). Increasing the science-based capacities, regulatory controls, and equitable accessibility to high-impact precision stem cell technologies will be crucial to help extend these treatments to all health systems.

1.3 Why Omics Technologies Matter

The shift towards precision therapeutics within the regenerative medicine landscape has been propelled by the development of multi-omics technologies. Stem cells form the basis of tissue engineering, and regenerative medicine, and omics technologies have broadened the understanding of the intricate molecular machinery controlling stem cell dynamics, disease progression, and clinical outcomes(Casado-Díaz, 2022). Multi-omics technologies have produced massive molecular data which has revolutionized the transition from conventional regenerative medicine to a more personalized and personalized medicine, shifting from a "one- size-fit-all approach" in regenerative medicine to a predictive and patient- centered regenerative medicine(Zhou et al., 2026).

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Genomics, transcriptomics, proteomics, epigenomics and metabolomics each provide distinct information. Integration of the different data provides a global picture of cell and disease function, helping to detect variants associated with a disease or condition of interest, understand changes in gene and protein expression, analyze dysregulated signaling pathways, and discover biomarkers that can predict disease progression and therapeutic response. These molecular markers are important in improving our understanding of stem cell biology and the optimization of stem cell-based therapeutic interventions(Vitorino, 2024).

Multi-omics technologies have transformed the use of stem cells in regenerative medicine, leading to a more personalized medicine, by providing new insights into disease mechanisms and potential therapeutic targets. For example, genetic information can be used to identify unique genetic differences among individuals and predict disease susceptibility, response to treatment, and potential side effects, while changes in the transcriptome and proteome can be used to better understand how stem cells differentiate, how tissues regenerate, and how cells interact with their microenvironment during these processes(Zayed et al., 2026).

Recently, the advancement of single-cell sequencing and spatial omics has provided unprecedented resolution in the analysis of cellular heterogeneity and interactions with cellular microenvironments, which are important in stem cell selection and quality control during cell manufacturing and in identifying novel molecular targets that can be modulated for therapeutic interventions(Ruta et al., 2024).

Moreover, integration of artificial intelligence (AI) and advanced bioinformatics in multi-omics technologies has enhanced the utility of multiomics in stem cell-based therapeutics. AI approaches have facilitated the identification of clinically relevant multi-omics signatures, prediction of therapeutic outcomes, and the development of evidence-based therapeutic approaches through an enhanced understanding of stem cell behavior and their interaction with their microenvironment. Integrating genomic, transcriptomic, proteomic, metabolomic and other information to identify multi-omics signatures that can be used to predict disease outcomes and clinical response has resulted in multi-omics being more clinically relevant in the development of personalized stem cell-based therapies(Wei et al., 2023).

Although there are advantages of using multi-omics technologies in regenerative medicine, challenges still persist in their implementation into standard clinical and research practice in many low- and middle-income countries (LMICs) due to high cost, low availability of platforms for next-generation sequencing, limited bioinformatics expertise, inadequate data storage and sharing, and many other reasons(Yek et al., 2022).

1.4 Why Focus on Low- and Middle-Income Countries (LMICs)

In the last two decades, regenerative medicine, stem cell biology, and multi-omics have progressed at a rapid rate. However, this success has not been evenly distributed globally. Most of it has happened in high-income nations, mainly thanks to long-term funding for biomedical science, sophisticated laboratory environments, favorable regulatory environments, and well-developed translational research pipelines. All of these have helped to move regenerative approaches from the bench to the bedside faster.

Conversely, most low- and middle-income countries (LMICs) still face major challenges that slow the development of regenerative science and prevent the delivery of new regenerative treatments to patients(Tahir & Tahir, 2025). It is important to consider the LMICs, not only because they encompass the majority of the world's population, but also because many people in these countries suffer from diseases (chronic diseases, infectious diseases, inherited disorders, and injuries) that may cause death or result in disability, where regenerative medicine may have an advantage(Grace, 2023). Still, funding for regenerative sciences is limited. Additionally, poor laboratory conditions, lack of scientific talent, fragmented regulations, and poor access to high-throughput sequencing and bioinformatics are

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limiting both the ability to do regenerative science and the delivery of regenerative therapies. This may lead to disparities in accessing precision medicines across the world(Huang & Guo, 2022). Even so, there are still opportunities in the LMICs in regenerative medicine. Genetically diverse populations, unique diseases, and growing investments in science and biotechnology may be an advantage for regenerative sciences. Moreover, there are new opportunities for global research, collaboration, technology transfer, and training that support regenerative science. These include the application of stem cell science and omic-based health care. With the help of proper regulations, funding, and scientific environments, the LMICs can become innovators, not just adopters, of regenerative therapies(Ogbogu & Albrecht, 2025). For this reason, regenerative medicine needs to be considered from the view of LMICs, so that we can identify both the opportunities for advancing regenerative sciences and the obstacles that prevent the global delivery of regenerative treatments, in order to allow the LMICs to access precision medicine and stem cell–based therapies. This review summarizes the opportunities and obstacles that stem cell science, multi-omics, and precision medicine may have for advancing regenerative therapies in LMICs by considering scientific advancements, technology, regulations, and economics.

1.5 Scope and Objectives of the Review

The integration of stem cell biology, multi-omics tools, and precision medicine is increasingly facilitating personalized treatment plans for regenerative medicine. However, despite rapid advancements in this area, the clinical application of stem cell therapies goes beyond new scientific breakthroughs. It requires an enabling environment consisting of sufficient research capacity, appropriate policies and regulatory frameworks, a skilled workforce, and equitable access to regenerative health care. While high-income countries have made substantial progress in many of these areas, challenges such as inadequate financial resources hamper regenerative research and translation of findings into routine clinical applications in many low- and middle-income countries (LMICs). To understand the state of regenerative medicine, it is important to take a holistic approach that encompasses both scientific discoveries, but also the healthcare infrastructure, regulatory and policy environment that enable their successful translation to the clinic (Doxzen et al., 2024).

In this review, we provide an overview of the role of stem cells in the context of precision regenerative medicine, highlighting how stem cell biology is coupled with emerging multi-omics (eg, genomics, transcriptomics, proteomics, metabolomics, epigenomics, etc.) approaches to facilitate more personalized regenerative therapies. We also summarize how other recent technological advances such as genome editing, tissue engineering, organoids, extracellular vesicles, artificial intelligence, and other related emerging technologies contribute to the current state of the art of regenerative medicine(Hoang et al., 2025). Our review highlights the current application of stem cell-based regenerative strategies in various major diseases and also summarizes our current understanding of the molecular basis of their therapeutic efficacy(Han et al., 2025).

Finally, we consider the unique challenges to regenerative medicine in LMICs and identify the scientific, technological, regulatory, socioeconomic, and healthcare environment for precision regenerative medicine to facilitate the growth and application of regenerative medicine in resource-limited settings. In doing so, we identify the opportunities for capacity building, global collaboration, and technology transfer to facilitate regenerative medicine innovation in the LMICs. We identify research gaps, and the current and future directions to develop and improve precision regenerative medicine that is both safe and effective in resource-limited regions(Anaya et al., 2025; Russa & Mtebe, 2026).

2. Stem Cell Biology: The Foundation of Regenerative Therapeutics

2.1 Fundamental Properties of Stem Cells

Self-renewal and differentiation are the two characteristics that differentiate stem cells from the rest. Stem cells have a remarkable ability to

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maintain their biological functions, and to maintain tissue throughout the life cycle. Due to these properties, stem cells can be used in regeneration and personalized medicine (Varzideh et al., 2023). Self-renewal is the property of stem cells in the process of self-replication (a series of cell division) while maintaining biological properties of the cell. Self-renewal allows stem cells to maintain their numbers, and thus providing them a steady supply to maintain and restore healthy tissues and cells after damage. Differentiation is another characteristic of stem cells that is triggered by environmental and intrinsic factors. It allows stem cells to generate new types of cells that can replace and/or recover damaged and injured tissues. It should be noted that not all stem cells participate in regeneration only by cell differentiation. Some MSCs may have the capacity to release various factors that have regenerative and immunoregulatory effects, including anti-inflammatory and angiogenic factors, that promote intrinsic tissue repair and regeneration. Therefore, self-renewal and differentiation are the main features of stem cells used in regenerative medicine(Harrell et al., 2021; Semba et al., 2020).

Self-renewal and differentiation are tightly regulated by each other and controlled by a signaling network and microenvironment within the niche (a niche in which stem cells live) to maintain the proper number of stem cells and their properties. Thus, self-renewal and differentiation are two main features of stem cells and may lead us towards advanced cell therapies and the use of stem cells combined with various omic technologies to implement the concept of personalized medicine (Aphkhazava et al., 2025).

2.2 Stem Cell Potency

The term "potency" defines a stem cell's capacity to differentiate and become the various types of specialized cells in the body. According to potency, stem cells are divided into the following:

- Totipotent
- Pluripotent
- Multipotent
- Oligopotent
- Unipotent

Knowing how powerful a stem cell population becomes important since it establishes whether it can be used in a particular research or therapeutic context. Knowledge of these categories sets a foundation for choosing the appropriate kind of stem cell for the study of regenerative medicine, disease, tissue engineering and even precision medicine(Riveiro & Brickman, 2020).

2.2.1 Totipotent Stem Cells

Totipotent stem cells exhibit the highest potential of being differentiated and can give birth to both the embryo and also the extraembryonic tissues including the placenta. They occur only at the earliest stage of embryo development; these cells can provide a great source for research on embryo and embryo development (Poliwoda et al., 2022).

2.2.2 Pluripotent Stem Cells

Pluripotent stem cells are able to differentiate into almost every single type of cell that is derived from the three embryonic germ layers of an individual, although they are not capable of forming the placenta or any other extraembryonic cells. There are two categories of Pluripotent stem cells, namely the Embryonic Stem Cells (ESCs) and the Induced Pluripotent stem cells (iPSCs). These cells are applied to disease modelling, drug discovery, developmental biology and even in generating of regenerative therapies for medical conditions(Shah & Khan, 2021).

2.2.3 Multipotent Stem Cells

Multipotent stem cells have a more restricted differentiation potential and can give rise to multiple related cell types from the specific tissue/organ. For instance, Hematopoietic stem cells may differentiate into all blood cell types and Mesenchymal stem cells (MSCs) differentiate into bone, cartilage, fat, and muscle cells. These cells have a significant role to play in tissue homeostasis and repair processes, thus are used in regenerative medicine and cell based therapies (Yadav, 2025).

2.2.4 Oligopotent Stem Cells

Oligopotent stem cells have greater restricted potency when compared to multipotent cells, in that they are able to produce only a restricted

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number of closely related cell types of a single tissue or organ system. Such examples include the progenitor cells that differentiate into a given blood or immune cells lineage when the cells have to become specialized in a specific manner for proper functioning(Rosner et al., 2023).

2.2.5 Unipotent Stem Cells

They have the most reduced potential of giving rise to only one type of the specialized cells with self-renewal ability. For example, skeletal muscle satellite cells and epidermal stem cells that play an important role in tissue homeostasis and regeneration(Mannino et al., 2022).

Stem cell potency forms an important basis of cell selection for both research as well as clinical purposes. Generally, stem cells with broad differentiation potential possess more flexibility in development, while cells with restricted potency are targeted towards tissue-specific homeostasis. Knowledge of the stem cell potency levels thus plays a key role in the design of a stem cell – based therapy and precision regenerative medicine(Hussen et al., 2024).

Table 1: Classification of Stem Cells According to Developmental Potency, Differentiation Capacity, and Clinical Applications

Potency	Differentiation Capacity	Example	Clinical Relevance
Totipotent	All embryonic and extraembryonic tissues	Zygote, early blastomeres	Developmental biology
Pluripotent	All cell types of the three germ layers	ESCs, iPSCs	Disease modeling, gene editing, regenerative therapies
Multipotent	Multiple cell types within one lineage	Hematopoietic stem cells, MSCs	Tissue regeneration, cell therapy
Oligopotent	A few closely related cell types	Myeloid and lymphoid progenitors	Hematopoiesis and immune regeneration
Unipotent	One specialized cell type	Muscle satellite cells, epidermal stem cells	Tissue maintenance and wound healing

2.3 Types of Stem Cells

Stem cells differ from each other with regard to their source of origin, biological features, and clinical applications. Therefore, each stem cell has its own pros and cons, and choosing the optimal stem cell for application in research and therapy depends on the goal of that research or therapeutic approach.

2.3.1 Embryonic Stem Cells (ESCs)

ESCs are pluripotent cells derived from the inner cell mass of the blastocyst stage of an embryo. This property gives them the ability to differentiate into any cell type arising from all three embryonic germ layers. Due to their high potential of differentiation and the fact that they self-renew indefinitely, ESCs are a valuable resource for research, regenerative medicine, drug development, and disease modeling. On the other hand, due to ethical concerns about embryo destruction, possible immune rejection following transplantation, and the risk of teratomas, their clinical applications are limited(Lewis et al., 2020; Ren et al., 2025).

2.3.2 Adult Stem Cells (ASCs)

ASCs are also known as somatic stem cells; they are tissue-specific stem cells found in many organs, such as the skin, adipose tissue, bone marrow, and central nervous system. They play a role in the growth and maintenance of the specific tissue in the body(Alkhatib, 2024). In contrast to ESCs, they are multipotent; i.e., they can only differentiate into a limited number of cell types. ASCs have the advantages of availability, low immunogenicity, and low ethical concerns. They, however, have limited differentiation potential and their proliferative capacity can decrease with age; these disadvantages can limit their regenerative efficacy(Alkhatib, 2024).

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2.3.3 Mesenchymal Stem Cells (MSCs)

MSCs are multipotent stromal cells that can be obtained from several tissue types, such as umbilical cord, adipose tissue, bone marrow, and dental pulp. Aside from their ability to differentiate into bone, cartilage, and adipose tissue, MSCs possess immunomodulatory and anti-inflammatory effects which are mainly attributed to their ability to secrete paracrine factors. Due to their safety profile, low immunogenicity, and regenerative potential, MSCs are extensively studied in clinical trials for treating various diseases such as autoimmune diseases, inflammatory disorders, osteoarthritis, and cardiovascular diseases (Costela-Ruiz et al., 2022; Kou et al., 2022).

2.3.4 Induced Pluripotent Stem Cells (iPSCs)

iPSCs are pluripotent cells obtained by reprogramming somatic cells using specific transcription factors. Like ESCs, these cells can differentiate into nearly all the human cell types, while circumventing many of the ethical concerns with ESCs. Their ability to be patient specific makes them valuable in areas such as drug screening, disease modeling, gene therapy, and personalized regenerative medicine. Nevertheless, issues like genomic instability, heterogeneity in reprogramming efficiency, and the potential for tumorigenicity have slowed their use in clinical practice (Dhaiban et al., 2025; Mao et al., 2022).

2.3.5 Perinatal Stem Cells

Perinatal stem cells are obtained from various perinatal tissue types, such as the amniotic membrane, amniotic fluid, placenta, and umbilical cord. These cells are easily accessible, have a low immune response, and are free of many of the ethical concerns related to embryonic cells. These cells show great therapeutic and regenerative potential and have drawn a significant amount of attention for possible tissue engineering and immune-mediated disorder treatments. While there has been a growing interest in the therapeutic use of these cells, there are currently no standardized isolation protocols in place. More clinical trials are also needed to establish the long-term safety and efficacy of these cells (Kulus et al., 2021).

In conclusion, stem cell types are biologically different and can differ in their suitability for therapeutic and research applications. Therefore, the choice of appropriate stem cell involves taking into consideration several factors, such as the biological and therapeutic properties of the cells, the goal of therapy, ethical concerns, and their immunological compatibility. The consideration of these factors will further the advancement of personalized regenerative medicine to meet the needs of different patients (Maraldi & Russo, 2022).

Table 2: Comparison of Major Stem Cell Types, Biological Characteristics, and Clinical Applications

Stem Cell Type	Source	Potency	Major Advantages	Major Limitations	Major Applications
ESCs	Blastocyst	Pluripotent	Unlimited differentiation	Ethical concerns, teratoma risk	Disease modeling, regenerative medicine
ASCs	Adult tissues	Multipotent	Easy isolation, low ethical concerns	Limited differentiation	Tissue repair
MSCs	Bone marrow, adipose tissue, umbilical cord	Multipotent	Immunomodulatory, low immunogenicity	Limited lineage potential	Orthopedics, autoimmune diseases

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iPSCs	Reprogrammed somatic cells	Pluripotent	Patient-specific, avoids embryo use	Genomic instability, tumorigenicity	Precision medicine, gene therapy
Perinatal Stem Cells	Placenta, umbilical cord, amniotic tissues	Multipotent	Readily available, low immunogenicity	Standardization challenges	Tissue engineering, wound healing

2.4 Stem Cell Niches

A stem cell niche refers to a specialized microenvironment that controls a stem cell's survival, self-renewal, quiescence, proliferation, and differentiation. Stem cells do not exist in isolation but constantly interact with their niche to maintain the normal function and regenerative capacity of tissues(Yushkov et al., 2025).

The stem cell niche comprises a combination of cell types, such as stromal cells, endothelial cells, immune cells, fibroblasts, and neighboring differentiated cells, and extracellular components, such as the extracellular matrix (ECM), growth factors, and cytokines. Cells communicate with each other directly through cell–cell contact and indirectly via soluble molecules (Farahzadi et al., 2023).

The ECM is a network of structural proteins, including collagen, laminin, and fibronectin, which forms a three-dimensional scaffold that maintains the structural integrity and mechanical stability of the niche. Growth factors, including transforming growth factor-β (TGF-β), fibroblast growth factors (FGFs), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF), as well as various cytokines, regulate stem cell function through complex signaling networks. Mechanical signals, such as matrix stiffness, fluid shear stress, and tensile forces, also play important roles in directing stem cell fate and function(Abdul-Al et al., 2021).

The precise interplay between cellular, molecular, and mechanical components within the niche regulates the balance between stem cell self-renewal and differentiation, thus maintaining tissue homeostasis. Disruption of the niche architecture or composition can lead to loss of regenerative capacity and contribute to aging, fibrosis, degenerative diseases, and cancer. Understanding the complex dynamics of stem cell niches is therefore essential for developing effective regenerative therapies and novel stem cell–based treatments(Busch et al., 2024).

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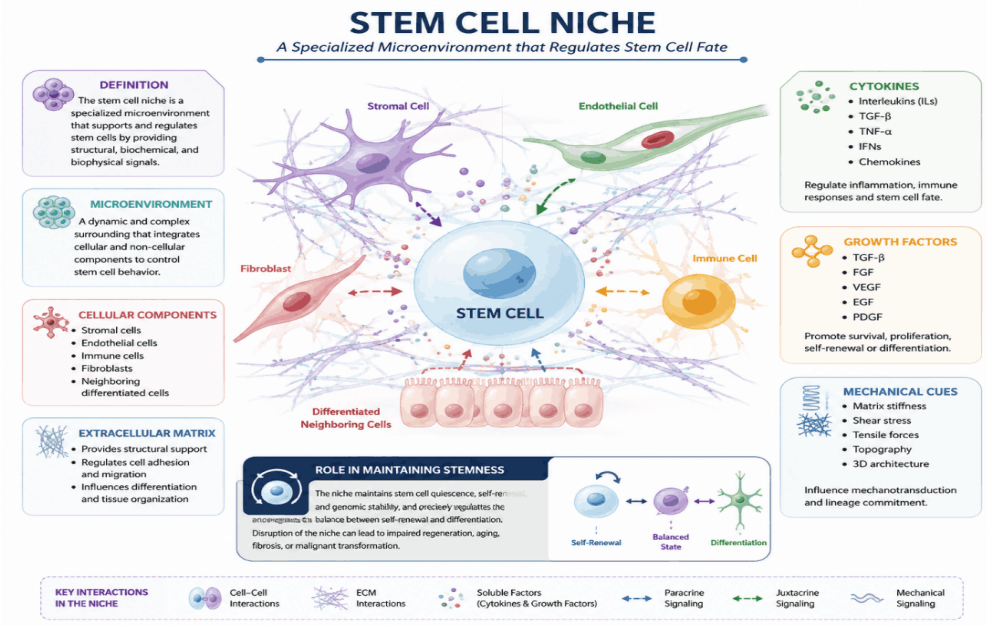


Figure 1. Stem cell niche as a specialized microenvironment regulating stem cell fate.

The stem cell niche comprises cellular components, extracellular matrix, cytokines, growth factors, and mechanical cues that collectively regulate stem cell quiescence, self-renewal, proliferation, differentiation, and tissue homeostasis through dynamic cell–cell and cell–matrix interactions.

2.5 Self-Renewal and Differentiation

Stem cell self-renewal and differentiation represent the hallmark characteristics that define the stem cell state and function. Self-renewal refers to the ability of stem cells to undergo repeated cell division while remaining undifferentiated, thereby maintaining the stem cell reservoir. This process allows stem cells to persist in tissues and produce specialized cell types for tissue maintenance and repair when needed (Borjesson & Overmann, 2022).

Stem cells can divide in two ways that impact self-renewal and differentiation. In symmetric division, stem cells produce two identical stem cells or two committed progenitor cells, thereby either expanding the stem cell pool or increasing the number of cells available for tissue growth and repair, respectively. Asymmetric division, which results in one daughter stem cell and one daughter committed progenitor cell, preserves the stem cell reservoir while generating cells for tissue regeneration(Mannino et al., 2022).

After cell division, stem cells begin to undergo lineage commitment, a process by which pluripotent or multipotent stem cells become progressively restricted in their developmental potential to generate specific cell types. This is accompanied by cell fate specification, which determines the ultimate identity of the cell as it transitions from an immature, undifferentiated state to a terminally differentiated, specialized phenotype. During this transition, cells undergo coordinated changes in gene expression and epigenetic status, allowing stem cells to follow defined developmental programs and differentiate into specific cell lineages, such as neural, mesenchymal, or hematopoietic cells, in response to specific internal and external cues (Aphkhazava et al., 2025).

Stem cell self-renewal and differentiation are tightly regulated by the stem cell niche and by highly conserved signaling pathways including Wnt/β-catenin, Notch, Hedgehog, TGF-β/BMP, PI3K/AKT, JAK/STAT, and Hippo-YAP pathways. These pathways play a crucial role in maintaining stem cell quiescence, survival,

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proliferation, self-renewal, and differentiation, thereby enabling stem cells to adapt to changes in the local microenvironment and maintain tissue homeostasis. Aberrant activation or inhibition of these pathways can lead to tissue dysfunction, aging, developmental disorders, fibrosis, and cancer. Thus, a thorough understanding of the molecular mechanisms that control stem cell self-renewal and differentiation is essential for developing regenerative and precision medicine approaches. The next section focuses on the major signaling pathways and their role in regulating stem cell behavior (Ahmadi et al., 2026; Zgeib, 2025).

3. Molecular Basis of Stem Cell Function

3.1 Genetic Regulation

Stem cell behavior whether cells stay undifferentiated, self-renew, or commit to becoming a specific cell type is governed by genetic regulation. This occurs within gene regulatory networks that keep stem cells in a pluripotent state while simultaneously triggering genes that define particular cell lineages when stimulated by signals, including those from development and the environment. Genetic regulation is critical for maintaining stem cells in proper numbers during tissue homeostasis and for their controlled differentiation during development and repair(Estrada-Meza et al., 2022; Krishnan et al., 2021).

Core genes such as OCT4, SOX2, and NANOG are the transcription factors that control the self-renewal and pluripotency of stem cells. They do this by upregulating genes involved in maintaining pluripotency and downregulating genes involved in cell differentiation. Other transcription factors including KLF4 and c-MYC cooperate with OCT4 and SOX2, forming the Yamanaka factors, to induce reprogramming of somatic cells into induced pluripotent stem cells (iPSCs) (Park et al., 2024). These transcription factors influence the rate of self-renewal and/or differentiation by controlling their target genes(Aguirre et al., 2023). The interplay between promoters, enhancers, transcription factors, and gene regulatory networks must also be carefully regulated. When stem cells differentiate, genes associated with pluripotency tend to be downregulated and genes involved in cell differentiation become upregulated in a tightly controlled order. Genetic regulation is, thus, a key feature of stem cell biology. This control ensures the generation of a large population of differentiated cells while mitigating against the risk of aberrant differentiation and malignant transformation(Ray-Jones & Spivakov, 2021).

Next-generation sequencing, single-cell sequencing, and genome-wide association studies have been instrumental in our current knowledge of the genetic control of stem cells. These technologies have helped identify genetic factors regulating stem cells, stem cell signatures, and polymorphisms associated with the development of certain diseases. Additionally, gene-editing technologies including CRISPR/Cas9 provide new approaches for the correction of disease-associated genetic mutations and the engineering of stem cells (Saba et al., 2021).

Understanding the genetic regulation of stem cells is therefore important in order to facilitate stem cell therapy. Integrating knowledge from these technologies with stem cell biology will help researchers better understand tissue growth and development while also serving as a framework for regenerative medicine of the future (Rajalekshmi & Agrawal, 2025).

3.2 Epigenetic Regulation

Epigenetic regulation controls the stem cell identity, self-renewal, survival, and differentiation without changing its DNA sequence. It functions via reversible modifications to control which genes are active and which are inactive, thereby maintaining stem cells as stem cells and facilitating the differentiation of stem cells into a particular cell type in response to intrinsic signals or cues from the environment. These modifications play a role in embryonic development, tissue regeneration, and reprogramming somatic cells to become pluripotent stem cells (He et al., 2021).

These mechanisms include:

- DNA methylation
- Histone modification
- Chromatin remodeling
- Non-coding RNAs

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DNA methylation is typically found in promoter regions and functions to inhibit the transcription of a gene. Histone modification involves the alteration of histone proteins via methylation and acetylation. Histone methylation typically restricts transcription while acetylation promotes transcription by regulating the accessibility of DNA (Giallongo et al., 2021). Chromatin structure also influences the transcription of a gene by modifying the chromatin and controlling DNA accessibility. Non-coding RNAs like microRNAs (miRNA) and long non-coding RNAs (lncRNAs) control gene expression post-transcriptionally. This can affect self-renewal of stem cells as well as their lineage differentiation or tissue regeneration. During reprogramming of cells, epigenetic remodeling restores the epigenetic status of a pluripotent stem cell in somatic cells (Ali et al., 2026).

Epigenomic profiling and high throughput sequencing have improved our knowledge of epigenetics of stem cells. Integration with other omic data sets, like genomics and transcriptomics, has enabled the discovery of new epigenetic factors and molecular markers related to stem cells and their therapy. These advances will lead to the further development of epigenetic therapy to improve the safety and efficiency of stem cell-based regenerative medicine(Tedesco et al., 2022).

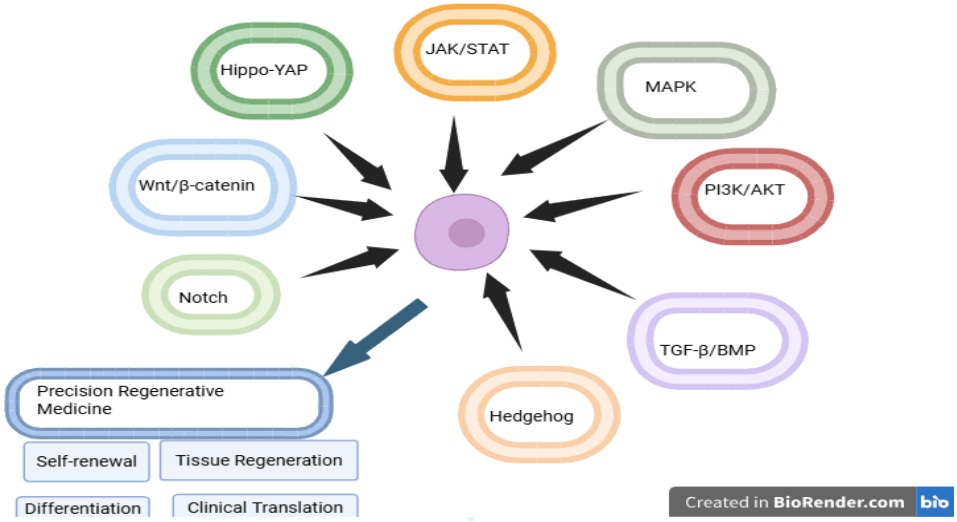


Figure 2. Major Signaling Pathways Regulating Stem Cell Fate in Precision Regenerative Medicine

A limited number of critical signaling pathways interact to direct stem cell fate. These pathways influence everything from self-renewal, proliferation, survival, commitment, and differentiation. For example, the Wnt/β-catenin pathway maintains stem cell identity in terms of self-renewal. The Notch and Hedgehog pathways are important for regulating stem cell fate determination, as well as basic development. The TGF-β/BMP pathway has a significant role in guiding lineage decisions. Additionally, the PI3K/AKT and MAPK pathways regulate cell survival and proliferation, which are particularly critical during tissue regeneration. The JAK/STAT pathway transmits cytokine signals involved in regenerative processes, while the Hippo-YAP pathway influences organ size, Mechan transduction, and the expansion of stem cells. Overall, the interplay among these diverse signaling cascades dictates tissue regeneration capacity as well as the success of regenerative therapies.

3.4 Transcription Factors

Transcription factors are critical players in the regulation of gene expression, essential for controlling stem cell behavior and identity. They maintain the intricate balance between self-renewal and differentiation, allowing stem cells to remain pluripotent or commit to a specialized

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lineage. Among many, a core set of transcription factors – OCT4, SOX2, NANOG, KLF4, and c-MYC – are essential for maintaining stem cell pluripotency and mediating reprogramming (Varzideh et al., 2023).

3.4.1 OCT4

OCT4 (POU5F1) is a key transcription factor that plays a major role in regulating embryonic stem cell pluripotency and self-renewal. It ensures the maintenance of stem cells in their undifferentiated state by controlling the expression of pluripotency genes, while its down-regulation or abnormal expression drives stem cells to differentiate into specific cell types. Therefore, tightly controlled OCT4 expression is crucial for the proper regulation of stem cells (Bakhmet & Tomilin, 2021).

3.4.2 SOX2

SOX2 interacts with OCT4 to control genes involved in stem cell pluripotency and self-renewal. In addition to its role in regulating stem cells, SOX2 is critical for neural development and is also required for maintaining induced pluripotent stem cells (iPSCs) (Zhu et al., 2021).

3.4.3 NANOG

NANOG is an important transcription factor involved in stem cell pluripotency; it inhibits spontaneous stem cell differentiation and helps maintain the undifferentiated state. Alongside OCT4 and SOX2, NANOG regulates the core transcriptional network that maintains the pluripotency of stem cells (Niu et al., 2021).

3.4.4 KLF4

KLF4 (Krüppel-like factor 4) regulates stem cell self-renewal, proliferation, differentiation, and homeostasis. It is one of the Yamanaka factors used for generating iPSCs from somatic cells and is involved in tissue regeneration and repair (Lacorazza, 2025).

3.4.5 c-MYC

c-MYC is a transcription factor that regulates a variety of genes involved in cell-cycle progression, protein production, cell metabolism, and cell proliferation. It is another Yamanaka factor that is critical for generating iPSCs from somatic cells. However, given its oncogenic potential, c-MYC expression requires careful control to ensure the safety of stem cell-based therapies (Meir & Li, 2021).

These transcription factors function as a regulatory network that controls stem cell fate by regulating pluripotency, self-renewal, and differentiation. Studies on these transcription factors have significantly contributed to stem cell biology and continue to support the development of regenerative medicine and precision therapeutics (Illi & Nasi, 2023).

Table 3. Key Transcription Factors Regulating Stem Cell Pluripotency, Self-Renewal, and Differentiation

Transcription Factor	Primary Function	Role in Stem Cell Biology
OCT4	Maintains pluripotency	Self-renewal and suppression of differentiation
SOX2	Regulates pluripotency genes	Stem cell maintenance and neural development
NANOG	Prevents spontaneous differentiation	Sustains the undifferentiated state
KLF4	Controls proliferation and self-renewal	Cellular reprogramming and tissue regeneration

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c-MYC	Promotes proliferation and metabolism	Enhances iPSC generation; associated with tumorigenic risk

4. Omics Technologies Driving Stem Cell Research

4.1 Genomics

Genomics has revolutionized the study of stem cells, providing unprecedented understanding of the molecular processes that govern stem cell identity, pluripotency, differentiation, and tissue regeneration. Next-generation sequencing (NGS) techniques allow for the identification of genetic variations, regulatory genes, and molecular pathways that regulate stem cell behavior and fate (Zhou et al., 2024). This knowledge has enhanced disease modeling, biomarker discovery, patient stratification, and personalized regenerative therapy development, making genomics a cornerstone of precision regenerative medicine(Gulati et al., 2025).

4.1.1 Whole Genome Sequencing (WGS)

Whole genome sequencing (WGS) involves sequencing the entire genome, including both coding and non-coding regions. In the context of stem cell research, WGS is used to identify genetic variants, structural variations, chromosomal abnormalities, and mutations that could potentially affect stem cell function, genomic stability, or safety in clinical applications. It is also used for the quality-control of stem cell lines and supports the development of patient-specific regenerative therapies (Merkle et al., 2022).

4.1.2 Whole Exome Sequencing (WES)

Whole exome sequencing (WES) focuses solely on the exons, which are the protein-coding regions of the genome, where most disease-causing mutations reside. Compared to WGS, WES is less expensive while still offering high diagnostic yield in diseases with genetic components. In regenerative medicine, WES aids in disease modeling, biomarker discovery, and the identification of candidates for personalized stem cell therapies (Kumar et al., 2025).

4.1.3 Genome-Wide Association Studies (GWAS)

Genome-wide association studies (GWAS) scan the genomes of large groups of individuals to identify genetic variants associated with particular traits, disease susceptibility, regenerative potential, and therapeutic outcomes. In stem cell research, GWAS has helped uncover genetic variants associated with stem cell properties, regenerative capabilities, and disease susceptibility. GWAS findings inform biomarker discovery, therapeutic target identification, and personalized regenerative medicine strategies (Salybekov et al., 2021).

Genomics contributes to the foundation of precision regenerative medicine through accurate genetic profiling, enhanced safety of stem cell-based therapies, and support for tailored therapeutic strategies. Combined with other omics technologies, genomics provides a comprehensive insight into stem cell biology and aids in the translation of regenerative therapies into clinical practice (Hu & Lazar, 2022).

Table 4. Genomic Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Purpose	Application in Stem Cell Research	Contribution to Precision Medicine
Whole Genome Sequencing (WGS)	Complete genome analysis	Detects genomic variants and structural alterations	Personalized therapy and genomic safety

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Whole Exome Sequencing (WES)	Analysis of coding regions	Identifies disease-causing mutations	Biomarker discovery and patient stratification
Genome-Wide Association Studies (GWAS)	Association of genetic variants with disease	Identifies susceptibility loci and therapeutic targets	Precision risk prediction and individualized treatment

4.2 Transcriptomics

Transcriptomics is defined as the study of the full complement of RNA transcripts that are produced by the genome, thus providing a dynamic snapshot of which genes are being expressed under specific biological conditions at specific times. Unlike genomics, which describes the genetic capacity of a cell, transcriptomics focuses on the genes that are actively expressed. This information has been instrumental in our understanding of stem cell heterogeneity, lineage specification, and cellular responses in the context of tissue regeneration. Consequently, transcriptomics is becoming an integral part of precision regenerative medicine (Ogi & Jin, 2023).

4.2.1 RNA Sequencing (RNA-seq)

RNA sequencing (RNA-seq) allows for high-sensitivity, comprehensive profiling of coding and non-coding RNA transcripts. RNA-seq has been extensively used in the context of stem cell research to study genes involved in stem cell maintenance, track differentiation, and identify biomarkers related to tissue regeneration. These transcriptomic data are used to enhance disease modeling and provide insights on how to design targeted regenerative therapies (Ogi & Jin, 2023).

4.2.2 Single-Cell RNA Sequencing (scRNA-seq)

Single-cell RNA sequencing (scRNA-seq) allows for profiling of gene expression at the single-cell level, which is important in identifying rare cell populations and assessing cellular heterogeneity not evident in bulk tissue analysis. The use of this technique has revolutionized stem cell research and is used to trace cell lineages, characterize differentiation pathways, and identify genes involved in development and regeneration. Additionally, scRNA-seq allows for biomarker identification and provides a means of assessing and optimizing stem cell-based therapies and tissue engineering approaches (Jovic et al., 2022).

4.2.3 Spatial Transcriptomics

Spatial transcriptomics is an integrated analysis of gene expression and spatial information to map RNA transcripts onto an intact tissue sample while retaining spatial resolution. Such data can provide valuable information regarding cell–cell interactions, stem cell niches, and tissue morphology in the context of regeneration. In regenerative medicine, spatial transcriptomics is being used to better understand tissue regeneration and to direct stem cell-based therapy to sites of injury to promote regeneration (Williams et al., 2022).

In summary, transcriptomic technologies provide a dynamic picture of gene expression and its correlation with cellular and tissue function. When used in combination with genomics and other multi-omics analyses, transcriptomic approaches can provide biomarker discovery, target identification, and the development of precision regenerative medicine.

Table 5. Transcriptomic Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Purpose	Application in Stem Cell Research	Contribution to Precision Medicine
RNA-seq	Global transcript profiling	Differential gene expression, biomarker discovery	Personalized therapeutic target identification

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Single-cell RNA-seq	Cell-specific transcriptomics	Cellular heterogeneity, lineage tracing	Precise cell characterization and patient stratification
Spatial transcriptomics	Spatial gene expression mapping	Stem cell niche and tissue architecture analysis	Optimization of regenerative therapies and tissue-specific interventions

4.3 Proteomics

Proteomics is defined as the study of the full complement of proteins expressed by the genome within a cell, tissue, or organ, providing direct insight into cellular function. Since proteins are primarily responsible for the vast majority of biological processes, proteomics has become very useful in studying the biology of stem cell signaling, regulation, differentiation, and tissue regeneration. In regenerative medicine, proteomics can identify protein biomarkers, therapeutic targets, and molecular changes related to stem cell function and regeneration, which makes proteomics a vital component of precision regenerative medicine (Mihai et al., 2021).

4.3.1 Mass Spectrometry (MS)

Mass spectrometry (MS) is the main tool in the proteomic analysis to identify, quantify, and characterize thousands of proteins, including post-translational modifications, at one time. MS-based proteomics is used in stem cell research for comprehensive analysis of the proteomic changes associated with stem cell self-renewal, differentiation, and maintenance of stem cell potency. These protein expression profiles provide insight into the molecular regulation of stem cell biology, in addition to being useful for biomarker discovery, as well as the monitoring of disease progression and response to therapy (Zayed et al., 2026).

4.3.2 Protein Interaction Networks

Protein interaction networks describe the functional relationships of proteins that collectively mediate biological processes. Since most cellular functions rely on the coordinated action of many interacting proteins, protein networks have become an important tool to elucidate the signaling molecules that regulate stem cell proliferation, differentiation, and tissue regeneration. Proteomic interaction networks integrated with other multi-omics data sets can be used to gain a systems view of stem cell biology and identify new therapeutic targets and to optimize regenerative therapy.

In general, proteomics can complement genomic and transcriptomic analyses by providing information regarding cellular function and protein activity. The combination of proteomics with other omics technologies can provide a better insight into regenerative biology and can be used to inform and develop stem cell therapy (Uversky & Giuliani, 2021).

Table 6. Proteomic Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Purpose	Application in Stem Cell Research	Contribution to Precision Medicine
Mass Spectrometry (MS)	Protein identification and quantification	Protein profiling, biomarker discovery, post-translational modification analysis	Therapeutic target identification and treatment monitoring
Protein Interaction Networks	Analysis of protein–protein interactions	Signaling pathway mapping, regulatory network analysis	Identification of key molecular targets and personalized therapeutic strategies

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4.4 Metabolomics

Metabolomics focuses on the entire collection of small-molecule metabolites in cells and tissues, giving a direct, in-the-moment look at how cells are functioning and metabolizing. Since a stem cell's job is deeply tied to how its metabolism works, studying its metabolites can tell us a lot about the processes behind stem cell self-renewal, differentiation, and repairing tissues. Studying metabolism and finding metabolites can help researchers figure out how to control stem cells, leading to better, more specific stem cell therapies in regenerative medicine (Bremers, 2026).

4.4.1 Metabolic Profiling

Metabolic profiling uses a quantitative measurement of small molecules in a stem cell, tissue, or body fluid to analyze the metabolic profile of different stem cell stages such as pluripotency, self-renewal, and differentiation. Identifying stem cell metabolites also can help researchers see how stem cell metabolism changes after exposure to a disease or to treatments. This allows us to better know how stem cells work and repair tissues (Bispo et al., 2021).

4.4.2 Metabolic Flux Analysis

Metabolic flux studies the movement and flow of metabolites within a living cell to look at how metabolic processes are changing. In stem cell research, this technique is used to find out what metabolites play a role in stem cell maintenance, specialization, and differentiation. These studies help researchers make cell cultures better, identify important metabolic pathways, and make stem cell-based treatments work better.

When used with the data of genomics, transcriptomics, proteomics, and other fields of omics, the study of small-molecule metabolites is used to figure out how cells react to both normal and abnormal conditions. The use of this data can be useful for finding biomarkers and better understanding how cell metabolism is controlled, leading to better and more specific stem cell-based therapies in regenerative medicine (Morganti et al., 2022).

Table 7. Metabolomic Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Purpose	Application in Stem Cell Research	Contribution to Precision Medicine
Metabolic Profiling	Quantification of cellular metabolites	Identification of metabolic signatures during self-renewal and differentiation	Biomarker discovery and therapeutic monitoring
Metabolic Flux Analysis	Measurement of metabolic pathway activity	Analysis of metabolic reprogramming and energy utilization	Optimization of regenerative therapies and prediction of treatment response

4.5 Epigenomics

Epigenomics is used to study the patterns of epigenetic markers that control whether genes are turned on or off, but the markers are not actually changes in DNA itself. The markers do not change the DNA, and they are what control how stem cells maintain their identity, maintain themselves, and develop into specific cell types. Studying these markers can help researchers better understand stem cell growth, development, and development of certain tissues. Epigenomics also helps researchers figure out how stem cells work and develop better regenerative medical treatments (Singla et al., 2023).

4.5.1 DNA Methylation Profiling

DNA methylation profiling studies which DNA bases have been methylated (added to a methyl group). Methylation does not change the DNA but it does help control how genes are expressed and helps cells make a choice to become a particular type of stem cell. In stem cell research, DNA methylation is used to help distinguish between the various stages of pluripotent stem cells and how they differentiate into cells of the body. It

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helps researchers understand the development of different tissues and stem cells. It can also be used to study cell cloning, find disease biomarkers, and analyze the quality and safety of stem cells for therapeutic use (Li et al., 2025).

4.5.2 Chromatin Accessibility and Histone Modification Analysis

Analyzing chromatin structure is a technique to help researchers see how stem cells' genes are turned on and off. These techniques include assays such as ATAC-seq to determine which parts of the genome are open for the transcription of RNA and ChIP-seq to determine the locations of histones, transcription factors, and other proteins on the DNA. Studying chromatin structure is used to help researchers better understand how to control stem cells, how they differentiate into specialized cell types, and how tissues are repaired. It can also be used to determine where genes are controlled and potential ways to control genes for regenerative treatments (Na et al., 2025).

The study of epigenetics is used to better understand how genes are controlled in response to normal and abnormal conditions. It is a useful complement to the study of genes and messenger RNA (mRNA). When integrated with other omics data, it can help researchers find new biomarkers and better understand how stem cells are controlled, leading to better regenerative medical treatments.

Table 8. Epigenomic Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Purpose	Application in Stem Cell Research	Contribution to Precision Medicine
DNA Methylation Profiling	Genome-wide methylation analysis	Monitoring pluripotency, differentiation, and cellular reprogramming	Epigenetic biomarkers and quality assessment
ATAC-seq / ChIP-seq	Analysis of chromatin accessibility and histone modifications	Identification of regulatory elements and transcriptional networks	Therapeutic target discovery and personalized regenerative therapies

4.6 Multi-omics Integration

It takes more than a single type of omics data to understand how stem cells work. Even though each type of omics data gives us useful knowledge, looking at the multiple different types together provides a wider look at the gene activity and pathways controlling stem cell maintenance, specialization, cellular identity, and tissue maintenance. Each type of omics data helps researchers learn something specific about cells and when these types of data are combined they are used to show the complicated interactions of gene activity that determine stem cell function and repair. Using the different types of omics data provides a much clearer understanding of stem cell activity than using just a single type of data (Theodorakis et al., 2024).

Multi-omics has been used for the last 10 years to learn more about the different variations in stem cell populations, the way the cells become specialized, and tissue repair. The technique helps researchers find biomarkers and therapies for stem cells. Integrating multi-omics with bioinformatics and artificial intelligence can help researchers better predict how stem cells will behave and be used to help guide clinical practice and make regenerative treatments (Chen et al., 2023).

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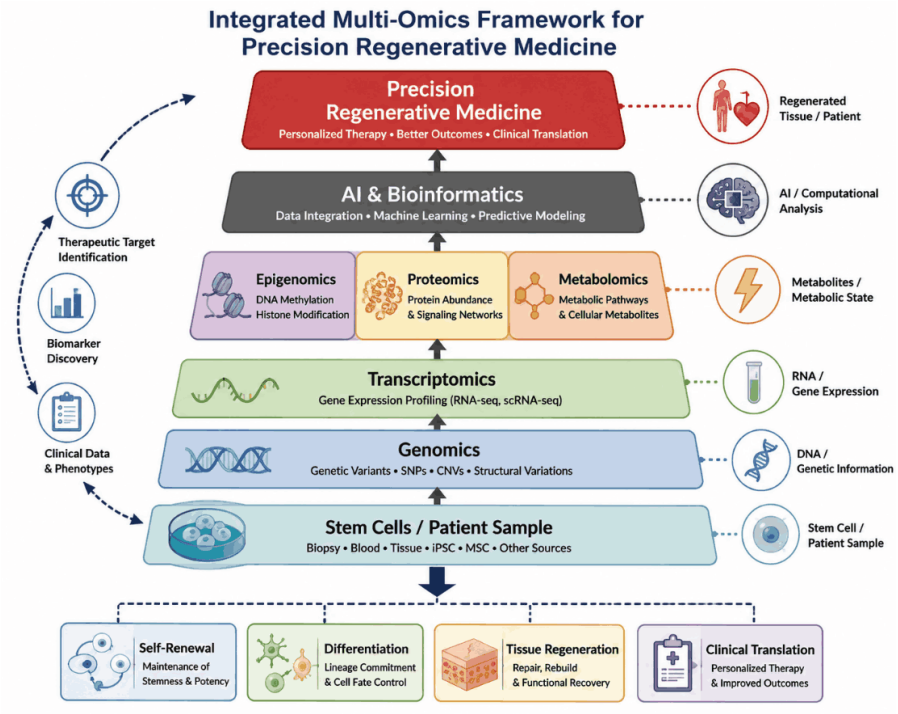


Figure:3 Integrated Multi-Omics and Artificial Intelligence Framework for Precision Regenerative Medicine

Stem cells or patient-derived biological samples undergo comprehensive multi-omics profiling, including genomics, transcriptomics, proteomics, metabolomics, and epigenomics, to capture complementary molecular information across different biological levels. These datasets are integrated using advanced bioinformatics and artificial intelligence approaches to identify biomarkers, characterize signaling networks, predict therapeutic responses, and uncover mechanisms governing stem cell self-renewal, differentiation, and tissue regeneration. This systems-level strategy supports patient stratification, personalized regenerative therapies, therapeutic target discovery, and accelerated clinical translation, providing a foundation for precision regenerative medicine across diverse healthcare settings.

5. Genetic Engineering and Advanced Biotechnology

The development of stem cell therapy is being propelled forward by recent technological advances in genetic engineering and biotechnology. The ability to precisely control cellular activity using genome editing, synthetic biology, organoid culture, and tissue engineering has improved disease modeling, drug development, and individualized therapies (Hussen et al., 2024). As a result, the move from stem cell therapy to clinical applications has improved, further facilitating the development of precision regenerative medicine.

5.1 CRISPR-Cas Systems

CRISPR-Cas systems have transformed genome editing by providing the potential for more specific, precise, and affordable gene manipulation than previous gene editing technology. These systems utilize a guide RNA to direct a CRISPR-associated (Cas) nuclease to specific DNA targets, where it causes a cut. This cut facilitates the deletion or insertion of genetic material, which in turn facilitates gene correction or silencing. CRISPR-Cas is utilized in stem cell research to correct genetic mutations associated with disease; study genes; model the human disease; and create patient-specific, tailored

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treatments for the cells. When used in conjunction with induced pluripotent stem cells (iPSCs), CRISPR-Cas technologies can enhance the practice of personalized regenerative medicine by enabling more precise gene correction and decreasing off-target effects to improve the safety of the therapeutic agent (Liu et al., 2022; Wang & Doudna, 2023).

5.2 Base Editing

Base editing is another genome editing technology that allows for the precise editing of individual DNA bases without producing a double-strand DNA break, as was required for CRISPR-Cas systems. Base editing enables high-fidelity editing while lowering DNA damage and off-target modifications compared with CRISPR-Cas-based methods. It can be used to correct single-nucleotide variants linked to genetic diseases. Base editing is a promising tool in regenerative medicine for safer and more precise therapy (Aliciaslan et al., 2026).

5.3 Prime Editing

Prime editing is another gene editing tool that does not require DNA donor template or cause double-strand DNA break. This system uses Cas9 nickase fused with reverse transcriptase and a pegRNA (prime editing guide RNA) that directs Cas9 to make the nicks and prime the template for the reverse transcription of new DNA into the target genome. Prime editing is a highly precise and flexible genome editing approach. Prime editing can be used to correct pathogenic mutations, study gene function, and design safer stem cell therapies (Zhao et al., 2023).

5.4 Gene Therapy

Gene therapy is a therapeutic approach aimed at addressing genetic or acquired diseases by the introduction, deletion, or modification of genetic material. Stem cells, which are able to self-renew, can be differentiated into the specific cell type required, and hence, make them a desirable platform for gene delivery. Gene therapy in combination with stem cell therapy has been applied to diseases affecting inherited blood diseases, immune diseases, metabolic disorders, neurodegenerative disease, and many others. This integration helps to further the field of personalized regenerative medicine (Cring & Sheffield, 2022).

5.5 Synthetic Biology

Synthetic biology is a multidisciplinary area of science that draws on the engineering principle to design, create, and construct biologically engineered systems that have predictable functions and are not present in nature. Through genetic circuit, regulatory circuit, and programmable genetic switches, stem cells can be modified to self-multiply, differentiate, or secrete therapeutics in response to certain biological events. As a result of the advances in this field, researchers have developed a better and more precise approach to cellular therapy and smart therapeutics of the future (Kortemme, 2024).

5.6 Organoids

Organoids are 3D tissue cultures generated from stem cells that resemble the structure and functionality of real organs. The organoid models have great utility to study human development, disease, and drug response. Patient-derived organoids can be applied in patient-specific disease modeling and drug testing, serving as a useful tool for translational research and precision medicine (Zhao et al., 2022).

5.7 3D Bioprinting

3D bioprinting represents a cutting-edge approach to regenerative medicine that utilizes 3D bioinks made of stem cells, biomaterials, and bioactive molecules to produce 3D structures of tissues (Loukelis et al., 2024). This method provides an accurate copy of a tissue structure for the purpose of tissue repair and regeneration, organ replacement, disease modeling, and patient-specific regenerative medicine (Tang et al., 2022).

5.8 Tissue Engineering

Tissue engineering is a multidisciplinary field that combines stem cells, biomaterials scaffolds, and bioactive molecules in order to restore, replace, and/or regenerate damaged or dysfunctional

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tissues. Biomaterial scaffolds are used to recreate the native ECM environment of the tissue of interest in order to induce attachment, proliferation, differentiation, and functionality of the seeded cells after transplantation. Biomaterials, scaffolds and bioprinting approaches have been used for bone, cartilage, skeletal muscles, neural tissues and epithelial tissues, making the field of tissue engineering one of the most promising areas of regenerative medicine (Zhao et al., 2021).

Table 9. Emerging Technologies and Their Applications in Stem Cell Research and Precision Regenerative Medicine

Technology	Primary Function	Stem Cell Application	Clinical Significance
CRISPR-Cas	Genome editing	Gene correction, disease modeling	Precision regenerative medicine
Base Editing	Single-base correction	Monogenic disease repair	High-precision gene therapy
Prime Editing	Precise genome modification	Mutation correction	Safer personalized therapies
Gene Therapy	Gene replacement/modification	Stem cell-based gene delivery	Treatment of inherited diseases
Synthetic Biology	Programmable cell engineering	Controlled differentiation	Smart regenerative therapeutics
Organoids	3D tissue models	Disease modeling, drug screening	Personalized medicine
3D Bioprinting	Fabrication of living tissues	Tissue reconstruction	Organ regeneration
Tissue Engineering	Stem cells + scaffolds	Functional tissue repair	Clinical tissue replacement

6. Stem Cells and Precision Medicine

The combination of stem cells, multi-omics, and genome engineering has led to advancements in the field of precision medicine in regenerative therapy, and to the development of patient-specific treatments. Nowadays, the clinical applications of stem cells in regenerative therapy for tissue repair and replacement have extended to patient-specific precision medicine by incorporating genomic information, molecular biomarkers, and clinical parameters into the treatment protocols for better personalized treatment outcomes (Azim et al., 2026). While stem cell approaches are utilized for disease modeling and regenerative therapeutic approaches, multi-omics is integrated as the basis for precision medicine to better characterize patients, diagnose disease states, and inform clinical treatment decision. These advances enable stem cell and precision medicine approaches to move the field of regenerative medicine toward a more personalized approach to patient care (Luce & Jean-Charles, 2025).

6.1 Personalized Cell Therapy

Personalized cell therapy is an emerging field in regenerative medicine where stem cells from a patient are used to repair or replace the specific cells in the patient that are either not functioning properly or have been damaged. With the development of induced pluripotent stem cells (iPSCs), genome engineering approaches, and tissue engineering approaches, individual patients can now receive genetically matched personalized cell therapy that minimizes the possibility of immune system rejection of donor cells and tissue replacement. Stem cell-based cell therapies have been applied in treating genetic conditions, cardiovascular disease, and neurological disease, and have potential in treating musculoskeletal tissue injury and degenerative disease to promote

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regeneration and personalized treatment outcomes (Clavellina et al., 2023).

6.2 Precision Diagnostics

Precision diagnostics combines the application of stem cell models and disease modeling in regenerative medicine approaches with multi-omics techniques in order to detect and better characterize various diseases. The identification of patient-specific molecular and cellular disease mechanisms allows for the detection of a disease in patients before symptoms develop. Patient-specific stem cell models can help better characterize disease mechanisms to aid in the early diagnosis and treatment, as well as guide personalized clinical decisions (Lopes et al., 2025).

6.3 Pharmacogenomics

Pharmacogenomics is the analysis of how genetic variations affect an individual's response to a drug or therapy. With the development of stem cell-based disease modeling, pharmacogenomic studies can be used to assess drug efficacy, drug safety, and personalized pharmacological dose for each individual patient, enabling personalized drug treatment with minimized side effects, and optimized pharmacological treatments for regenerative medicine therapy (Palasantzas et al., 2023).

6.4 Biomarker Discovery

The combination of stem cell disease modeling approaches with genomics, transcriptomics, proteomics, and metabolomics can help identify and validate biomarkers of tissue regeneration, disease progression, and drug response to assist in patient stratification, treatment monitoring, and to predict disease outcomes, leading to personalized and precision regenerative medicine (Subhan).

6.5 Patient-Specific iPSC Models

Patient-specific iPSC models are the gold standard in precision medicine since they allow for the maintenance of the patient's genetic background together with the cells' pluripotent capacity. In addition, patient-specific iPSC models can be applied in disease modeling, drug screening, genome editing, and toxicity testing prior to clinical use. Therefore, patient-specific iPSC models enable precision of treatment with a lower dependence on traditional animal models and immortalized cell lines (Aboul-Soud et al., 2021).

6.6 Digital Medicine and Artificial Intelligence

Digital medicine and artificial intelligence (AI) are also applied in the broader framework of precision regenerative medicine to increase the possibilities for disease management. AI tools can integrate, process, and mine clinical data, images and multi-omics data for the identification of disease signatures and biomarkers, prediction of stem cell fate, and selection of personalized treatments. These tools have the potential to improve clinical decision-making, refine patient stratification and prognoses, and hasten the clinical translation of stem cell therapies (Silva-Sousa et al., 2025).

Overall, stem cell technologies, multi-omics, genome editing, and digital medicine have changed the face of precision medicine as they enable more personalized approaches for diagnosis, treatment, and management of diseases. We anticipate that the continued developments and applications in the stem cell field, multi-omics, genome engineering, and digital medicine will lead to better patient outcomes, less complications, and better patient access to precision regenerative medicine across the globe.

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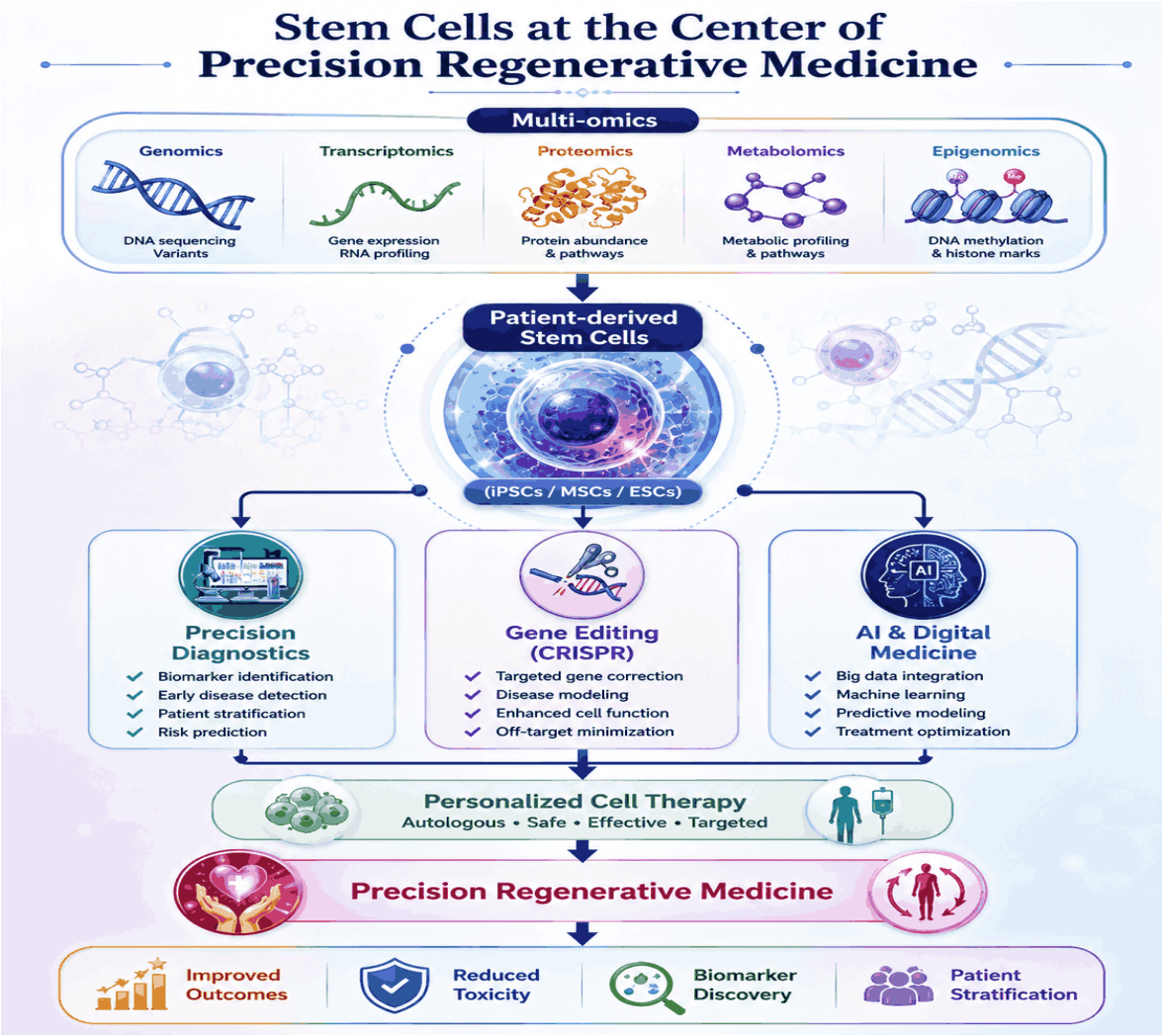


Figure 4. Stem cells anchor the field of precision regenerative medicine conjunction with multi-omics technologies (genomics, transcriptomics, proteomics, metabolomics, and epigenomics), scientists can interrogate patient stem cells, including iPSCs, MSCs, and ESCs. Combining these data can facilitate improved diagnostics, streamlined CRISPR editing of genes, and the use of AI-driven digital medicine to detect new biomarkers, disease modeling, patient stratification, and treatment decision making. Together, these tools empower development of patient-specific cell therapies that can enhance therapy outcomes, reduce toxicity, facilitate biomarker discovery, and maximize clinical outcomes.

7. Clinical Applications of Stem Cells in Precision Regenerative Medicine

Progress in stem cell research, multi-omics technologies, and genetic engineering have allowed for the expansion of the regenerative medical possibilities of the use of stem cells in the treatment of patients. Stem cell–based therapies could be used to repair or replace damaged tissue, to regulate immune responses, and to restore function of damaged organs. Stem cell therapy, if applied together with the precision medicine approach, can allow the stem cell–based therapy to be personalized to each individual patient based on the individual's molecular and clinical features, which would lead to an increased therapeutic efficacy and safety.

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7.1 Cancer

Stem cell–based therapies are also increasingly utilized for cancer research and in precision oncology. For example, patient-derived tumor organoids, engineered immune cells, and iPSC-derived cancer cell lines allow the investigation of tumor biology, testing of drug response and the identification of therapeutic targets. Hematopoietic stem cell transplantation is the current standard treatment for a number of hematological malignancies, while multi-omics and genomic profiling are employed in treatment selection and prognosis (El-Tanani et al., 2025).

7.2 Neurological Disorders

Stem cell–based therapies are currently being evaluated for neurological disorders such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and spinal cord injury. Neural stem cells, mesenchymal stem cells (MSCs), and neurons derived from iPSCs could be used to replace injured tissue, diminish neuroinflammation, and promote the recovery of neurological functions. Furthermore, stem cell-derived models could be applied in disease modeling and the testing of personalized treatments (Rahimi Darehbagh et al., 2024).

7.3 Cardiovascular Disease

Cardiovascular diseases remain one of the leading causes of morbidity and mortality globally, and the regenerative therapy of the heart is thus of particular interest in stem cell research. Studies are currently exploring how well mesenchymal stem cells, cardiac progenitor cells, and induced pluripotent stem cell-derived cardiomyocytes can repair heart tissue, rebuild blood vessels, and restore function after a heart attack. Precision medicine also helps identify which patients are most likely to respond positively to these treatments (Bakinowska et al., 2024; Tsai & Sun, 2024).

7.4 Diabetes

A major hurdle in diabetes care is the need for functional beta cells, which produce insulin. Researchers have developed methods using stem cells to generate pancreatic beta cells from pluripotent stem cells, offering new prospects for regeneration. When these cell types are coupled with patient-derived iPSCs and the latest advances in genetic engineering, they may help create new personalized treatments that better regulate blood glucose and reduce the need for long-term insulin therapy (Kerper et al., 2022; Wang et al., 2022).

7.5 Musculoskeletal Disorders

Stem cells have proven useful in treating a wide range of musculoskeletal conditions, ranging from osteoarthritis to cartilage damage to broken bones to tendon diseases to torn muscle fibers. Mesenchymal stem cells are useful in these cases because they have the ability to differentiate into bone, cartilage, and connective tissue, among other things. Additionally, the development of biomimetic scaffolds using 3D bioprinting and tissue engineering is improving tissue regeneration and promoting functional recovery (Pal et al., 2024; Trapana et al., 2024).

7.6 Autoimmune Diseases

The immunomodulatory properties of mesenchymal stem cells have been explored not only to treat regenerative diseases but also to treat autoimmune diseases like rheumatoid arthritis, lupus, and multiple sclerosis. These treatments might be helpful in lowering the immune response against disease and promoting tissue healing. Precision medicine is used to identify patients who are most likely to benefit from the therapy(Zeng et al., 2022).

7.7 Ophthalmology

The ease of access to this organ combined with its partial immune privilege make the eye a good target for regenerative therapies. Stem cell-based treatments for eye diseases like degenerative retinal disease, macular degeneration, corneal damage, and certain genetic eye conditions are currently being tested. Furthermore, stem cell disease models created from a patient's own cells could be utilized for disease modeling and personalized therapy (Ajgaonkar et al., 2023).

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7.8 Rare Genetic Disorders

Single gene disorders lend themselves well to regenerative medicine. Patient-derived iPSCs and genome editing have been used by scientists to investigate rare disease pathogenesis, to test potential drug compounds, and to develop individualized therapies. Significant progress has been made in treating sickle cell disease, beta thalassemia, Duchenne muscular dystrophy, and certain metabolic diseases. These medical applications demonstrate the breadth of regenerative medicine and its efficacy against a variety of conditions. By integrating multi-omics technologies and genome engineering into regenerative medicine strategies, clinicians and researchers may be able to provide more precise, safe, and effective treatment options for patients. Ongoing developments in both pre-clinical and clinical translational research will hopefully speed up the incorporation of stem cell-based precision medicine into clinical practice (Parvatam et al., 2025; Sun et al., 2017).

Table 10. Clinical Applications of Stem Cells in Precision Regenerative Medicine

Disease Area	Stem Cell Type(s)	Primary Therapeutic Goal	Precision Medicine Contribution
Cancer	HSCs, iPSCs, organoids	Hematopoietic restoration, drug screening	Precision oncology and biomarker-guided therapy
Neurological Disorders	Neural stem cells, MSCs, iPSC-derived neurons	Neural repair and neuroprotection	Patient-specific disease modeling
Cardiovascular Disease	MSCs, cardiac progenitor cells, iPSC-cardiomyocytes	Cardiac regeneration and angiogenesis	Individualized treatment optimization
Diabetes	ESC/iPSC-derived β-cells	Restoration of insulin production	Personalized regenerative therapy
Musculoskeletal Disorders	MSCs	Bone, cartilage, tendon, and muscle repair	Tissue engineering and biomaterial integration
Autoimmune Diseases	MSCs	Immunomodulation and tissue repair	Precision immunotherapy
Ophthalmology	ESC/iPSC-derived retinal cells	Retinal and corneal regeneration	Personalized ocular therapeutics
Rare Genetic Disorders	Patient-derived iPSCs	Gene correction and disease modeling	Genome editing and individualized therapy

8. Immunology of Stem Cell Therapy

The efficacy of stem cell-based regenerative therapies relies on not only regenerative potential but also immune-mediated interactions. Stem cells cross-talk with innate and adaptive immune cells and modulate immune responses, inflammation, tissue repair, and immune tolerance. These stem cell–immune interactions are key to optimizing engraftment, preventing rejection, and achieving therapeutic outcomes in precision regenerative medicine (Li et al., 2021).

8.1 Stem Cell–Immune Interactions

Stem cells interact with innate and adaptive immune cells including macrophages, dendritic cells, NK cells, T cells, and B cells, and with immune mediators to modulate inflammation, tissue repair, and regeneration. The immune-mediated inflammatory profile is an important regulator of stem cell efficacy in regenerative medicine (Sadeghi et al., 2025).

8.2 Immunomodulation

Immunomodulation is a key mechanism by which stem cells exert therapeutic effects, mediated by the secretion of cytokines, chemokines, growth factors, and extracellular vesicles to regulate inflammation, repair tissue, and restore immune homeostasis. Immunomodulatory effects of stem cells are increasingly recognized as a promising

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therapeutic strategy to treat inflammatory, autoimmune, and degenerative conditions and reinforce the application of stem cells in precision regenerative medicine (Li et al., 2023).

8.3 MSC Immunobiology

Mesenchymal stem cells (MSCs) are the most investigated population of cells for immune regulation in regenerative medicine. MSCs inhibit T- and B-cell responses, impair dendritic cell differentiation, and alter the polarization of macrophages. Low expression of class II MHC and costimulatory molecules reduces their immunogenicity, making MSCs suitable for clinical translation for allogeneic administration and treatment of inflammatory and autoimmune diseases (Maldonado et al., 2023).

8.4 Immune Rejection

While stem cells can be powerful tools for regenerative medicine, immune rejection remains a major hurdle in clinical translation. Immune recognition of the transplant can cause graft rejection, resulting in impaired graft survival and loss of therapeutic efficacy. Current strategies to reduce immunogenicity include HLA matching, immunomodulation, genome editing, and patient-specific iPSCs (Dhaiban et al., 2025).

8.5 Inflammatory Microenvironment

The inflammatory microenvironment is critical for stem cell therapy and is a key factor determining cell viability, cell homing, cell differentiation, and tissue integration. Although controlled inflammation promotes regeneration, chronic inflammation is deleterious and prevents cell survival and regeneration. Ongoing development of biomaterials, immunomodulatory agents, and tissue engineering strategies that modulate the inflammatory microenvironment is expected to facilitate more effective cell therapy in regenerative medicine (Chen et al., 2026).

Immunomodulation by stem cells is essential for the clinical efficacy of cell therapy and represents a crucial component of regenerative medicine. Harnessing an interdisciplinary approach that combines stem cell science with immunology, omics technologies, and precision medicine can enable the generation of immune-compatible stem cell derivatives and improved regenerative outcomes, advancing the future of regenerative medicine. The study of immune interactions between stem cells and host tissues is essential to the future clinical success of stem cell–based regenerative approaches, including overcoming barriers to effective immunomodulation and transplant.

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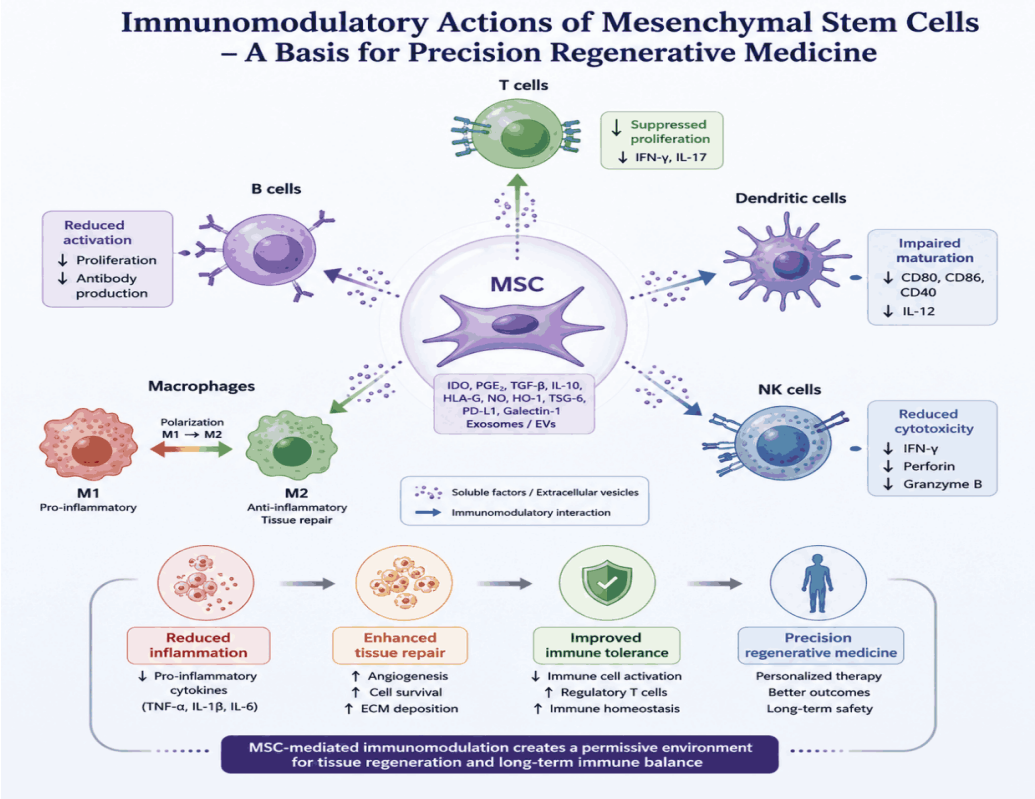


Figure 5. Immunomodulatory mechanisms of mesenchymal stem cells (MSCs) in precision regenerative medicine. MSCs regulate both innate and adaptive immune response by suppression of T and B cells, inhibition of DC maturation, inhibition of NK cell cytotoxic activity, and regulation of macrophage phenotype from the pro-inflammatory M1 to anti-inflammatory M2. These regulatory mechanisms reduce inflammation, repair tissues, facilitate tolerance of immunity, and lead to the development of the precision regenerative medicine.

9. Translational Challenges in Low- and Middle-Income Countries (LMICs)

Despite the rapid developments in stem cell research, the availability of multi-omics data, and the advent of precision medicine, the use of these new technologies in daily practice still varies in different regions of the world. Low- and middle-income countries (LMICs) face significant scientific, economic and healthcare barriers to regenerative medicine. Overcoming these barriers will increase access to and benefits of precision medicine, especially for stem cell-based therapies, around the globe (Ogbogu & Albrecht, 2026).

9.1 Infrastructure

A well-established research laboratory, Good Manufacturing Practice (GMP) facility, hospital with advanced clinical care units and genomic sequencing capability are important for regenerative medicine to become an available technology. Limited laboratory infrastructure is a common concern in many LMICs, making the development, clinical testing and translation of stem cell therapies a major challenge. Strengthening research infrastructure in LMICs and facilitating access to advanced technologies will accelerate the progress in this area of regenerative medicine (Doxzen et al., 2024).

9.2 Funding

The conduct of stem cell research and implementation of regenerative and precision medicine requires continuous funding for basic and translational research as well as technology

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development. However, limited funds for research, lack of local funds and dependence on foreign funding along with other national health priorities are delaying the progress in the research and clinical translation of stem cell therapies. In order to facilitate the research and implementation of stem cell therapies, governments and international organizations are required to prioritize regenerative medicine research, funding and implementation with greater collaboration and public–private partnership (Moreno et al., 2026).

9.3 Workforce

The advancement of regenerative medicine will depend on a skilled and diverse research workforce, including stem cell biologist(s), clinicians, bioinformatician(s), engineer(s), regulatory and translational specialist(s). There is a lack of human resources in the field of stem cell sciences in many LMICs and few opportunities for advanced training. Efforts to strengthen education and training and the creation of capacity will be the keys to developing a workforce that will sustain regenerative medicine research (Doxzen et al., 2024).

9.4 Regulatory Frameworks

Effective regulation is necessary for the safe and ethical application of stem cell technologies and their translation to clinical use. This includes cell and gene manufacturing, clinical trials, the use of genome editing and clinical trials using other translational technologies. While regulatory frameworks are developing, many LMICs do not have adequate regulation of regenerative medicine practices, making translation to clinical use and production difficult. In this regard, harmonized regulation and guidelines will enable safe innovation while building public confidence (Rouce & Grilley, 2025).

9.5 Ethical Issues

There are several concerns about the ethical, legal and social implications of stem cell therapies in the areas of genomic data, biobanks, genome editing and embryonic stem cell (ESC) research and therapy. Different countries have different rules and capacities when it comes to ethical regulation of these technologies. The establishment of appropriate regulations that align with international best-practices to ensure good practices and build public confidence will require greater emphasis in research governance (Marei, 2025).

9.6 Cell Manufacturing

To translate stem cell therapies to clinical applications, the stem cell products should be manufactured under Good Manufacturing Practice conditions with consistent quality and safety. Access to modern technology and GMP-certified facilities is limited in many LMICs. Increasing regional production will reduce the dependence on imported stem cell products and will increase the availability and affordability of stem cell therapies (Mukherjee, 2025).

9.7 Biobanking

High-quality samples are key for the advancement of precision and regenerative medicine and biomarker discovery. However, the establishment of biobanks with adequate sustainability and governance policies, data management, infrastructure and sample viability remains a challenge. National and regional biobanks with adequate funding and good governance will promote the quality of translational research and collaboration internationally (Valdés & Lecaros, 2024).

9.8 Quality Control

Ensuring safety and efficacy in stem cell manufacturing requires rigorous quality control measures covering genomic stability, donor screening, cell characterization, sterility assurance, and product consistency checks. The scarcity of quality control resources and lack of quality assurance standards in many LMICs can negatively affect the quality, efficacy, and safety of stem cell products. Implementing international quality standards will be helpful in achieving regulatory approvals and improving clinical outcomes (Wang & Du, 2026).

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9.9 Cost

Expensive genomic sequencing, genome editing, cell manufacturing, and personalized treatment costs are barriers that impede the expansion of regenerative medicine in LMICs. Decreasing costs for regenerative medicine by means of technology, localization of the production, and the production scale will be crucial for affordability and long-term success of precision regenerative medicine (Yamada et al., 2021).

9.10 Access to Precision Medicine

Limited access to precision medicine in LMICs has been noted because of insufficient reimbursement for genomic and regenerative technologies, the lack of trained professionals, as well as a dearth in genomics laboratories and molecular diagnostics infrastructure. Increasing the capacity for precision diagnostics, digital health, and genomic medicine will be essential in improving availability of new regenerative medicine interventions (Turner et al., 2025).

9.11 Health Equity

The achievement of health equity is the foundation of implementing precision regenerative medicine. Geographic and socioeconomic inequities and variations in access to health care remain impediments to the availability of stem cells and molecular diagnostics for many underserved populations. Efforts to reduce disparities, in the areas of access to affordability, technology transfer, sustainable funding, and international health initiatives will have to be initiated to achieve equity through governmental, academic, non-governmental, private, and international collaborations.

To address the obstacles confronting LMICs, it will take coordinated collaboration from governments, the public sector, healthcare and research communities, regulatory authorities, and the private sector. By investing strategically in healthcare and research infrastructure, health workforce education and training, regulatory infrastructure, local capacity building for stem cell production and technology transfer via South–South and public–private partnerships, and international research collaborations, countries can accelerate the translation and deployment of precision regenerative medicine, which will ultimately result in safer and equitable healthcare outcomes for all LMICs. Tackling these barriers will ensure that new scientific findings lead to effective therapies that are widely available and will also help to address disparities in regenerative healthcare worldwide.

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Figure 6. Translational challenges and enabling strategies for precision regenerative medicine in low- and middle-income countries (LMICs). Precision regenerative medicine in LMICs is impeded by interconnected challenges, including lack of infrastructure, funding, personnel, regulations and ethics, lack of stem cell manufacturing/biobanking, lack of QC, expenses, limitations on access to precision medicines, and inequalities in health. To accelerate translation of stem cell therapies safely, efficiently and with equitable access, coordinated investment and implementation of these enabling approaches are essential: improved infrastructure, sustainable funding, improved personnel training and recruitment, harmonized regulations and ethics, GMP stem cell manufacturing, biobanks, quality control and management, access to precision medicines, international collaboration.

10. Opportunities in Low- and Middle-Income Countries (LMICs)

These challenges notwithstanding, LMICs are rich opportunities for the further development of precision regenerative medicine. The genetic heterogeneity of LMIC populations could provide the opportunity for identifying disease-specific biomarkers and disease progression indicators, and discovering novel treatments. Furthermore, the size and genetic heterogeneity of these populations allow for translational and clinical studies that are difficult or impossible to carry out in homogenous populations found elsewhere. Public-private partnerships, South-South collaborations and international research collaborations could help to build scientific capacity, transfer of technology and resources between regions and countries and facilitate their exchange. The development of artificial intelligence, digital platforms and regional stem

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cell manufacturing hubs provide opportunities for practical, scalable and cost-effective means of addressing some of the limitations to access, affordability and deployment of stem cell based precision regenerative medicine in resource constrained settings (Aguilar-Gallardo & Bonora-Centelles, 2024).

11. Emerging Technologies

In the future, precision regenerative medicine will undoubtedly be transformed by novel technologies, particularly with regard to disease modelling, therapeutic development, and clinical translation. These include single-cell multi-omics and spatial omics technologies, which provide new information on cellular diversity, tissue architecture, and disease mechanisms; artificial intelligence, which facilitates multi-omics integration, biomarker discovery, and predictive modeling for personalized medicine; digital twins and new editing technologies such as CRISPR, which improve therapeutic development and precision; and cell-free therapeutic modalities, such as extracellular vesicles and exosomes, as well as organ-on-a-chip technology for more physiological modeling of human systems, and for drug discovery and therapeutic development (Yiu et al., 2025).

12. Knowledge Gaps and Future Directions

Although major strides have been made in the field of precision regenerative medicine, further research must be conducted to address some of the scientific and translational hurdles before the full potential of these approaches can be realized in clinical practice. Specifically, the large-scale validation in the clinic, standardization of multi-omics data acquisition and analysis, long-term safety and efficacy evaluations, as well as biomarker development will need to be furthered. This will require an expansion in research platforms, biobanks, computational infrastructure and bioinformatics expertise, especially in LMICs, to further support and facilitate clinical implementation. In addition, regulatory and governmental standardization and international collaborations will need to be prioritized for promoting innovation, increasing accessibility and global implementation of precision regenerative medicine (Dahiya et al., 2025).

13. Conclusion

The convergence of stem cell sciences and multi-omics, AI, and bioinformatics with precision regenerative medicine could transform modern medicine by facilitating more personalized approaches to therapy. It may enable us to understand disease mechanisms, identify predictive biomarkers, develop better patient stratification, and maximize therapeutic efficacy and safety.

Despite the fact that the translation of precision regenerative medicine poses unique challenges for LMICs, LMICs also have certain advantages—such as their genetic diversity, large populations, and expanding research capabilities. To fully realize the potential of precision regenerative medicine in LMICs, more efforts need to be made to invest in infrastructure, harmonization, capacity building, access, and international/regional collaboration. We can bridge the gap from molecular to clinical translation and ultimately enable a future where precision regenerative medicine brings better healthcare to all, regardless of where they live in the world.

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REFERENCES:

Abdul-Al, M., Kyeremeh, G. K., Saeinasab, M., Heidari Keshel, S., & Sefat, F. (2021). Stem cell niche microenvironment. *Bioengineering*, *8*(8), 108.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Aboul-Soud, M. A., Alzahrani, A. J., & Mahmoud, A. (2021). Induced pluripotent stem cells (iPSCs)—roles in regenerative therapies, disease modelling and drug screening. *Cells*, *10*(9), 2319.

Aguilar-Gallardo, C., & Bonora-Centelles, A. (2024). Integrating artificial intelligence for academic advanced therapy medicinal products: challenges and opportunities. *Applied Sciences*, *14*(3), 1303.

Aguirre, M., Escobar, M., Forero Amézquita, S., Cubillos, D., Rincón, C., Vanegas, P., Tarazona, M. P., Atuesta Escobar, S., Blanco, J. C., & Celis, L. G. (2023). Application of the Yamanaka transcription factors Oct4, Sox2, Klf4, and c-Myc from the laboratory to the clinic. *Genes*, *14*(9), 1697.

Ahmadi, Y., Mohammed, T., Abolhasani, S., Abdullah Hamad, S., & Faiq, T. (2026). Dysregulation of the Cyclin D/E2F activity as a core mechanism driving cancer stem cell plasticity and cell cycle dynamics. *Cell Cycle*, *25*(1), 1-29.

Ajgaonkar, B. S., Kumaran, A., Kumar, S., Jain, R. D., & Dandekar, P. P. (2023). Cell-based therapies for corneal and retinal disorders. *Stem cell reviews and reports*, *19*(8), 2650-2682.

Ali, T., Ali, F., Hussain, A. F., Osee, T., & Alam, W. (2026). GENOMIC AND EPIGENETIC MODIFICATIONSCONTROLLING STEM CELL DIFFERENTIATION ANDREGENERATIVE POTENTIAL IN EARLY DEVELOPMENT: A COMPREHENSIVE CRITICAL REVIEW. *Pakistan Journal of Medical & Cardiological Review*, *5*(1), 579-597.

Aliciaslan, M., Erbasan, E., Erendor, F., & Sanlioglu, S. (2026). Advances in CRISPR base editing: from molecular evolution to therapeutic applications in genomic medicine. *Journal of Cellular and Molecular Medicine (Online)*, *30*(8).

Alkhatib, A. J. (2024). The Role of Adult Stem Cells in Tissue Healing and Therapeutic Applications. *PSM Microbiology*, *9*(3), 42-61.

Anaya, J.-M., Herrán, M., & Pino, L. E. (2025). Challenges and opportunities for precision medicine in developing nations. *Expert Review of Precision Medicine and Drug Development*, *10*(1), 1-15.

Aphkhazava, D., Sulashvili, N., & Tkemaladze, J. (2025). Stem cell systems and regeneration. *Georgian Scientists*, *7*(1), 271-319.

Azim, M. M., Bhajan, S. K., Park, J. H., Abass, K. S., Rahman, A., Choi, M., Choi, J., Park, S., Kim, H. J., & Akter, S. (2026). Stem cell-derived organoids for cancer therapy: Precision medicine and drug selection. *International journal of molecular sciences*, *27*(7), 2954.

Bakhmet, E. I., & Tomilin, A. N. (2021). Key features of the POU transcription factor Oct4 from an evolutionary perspective. *Cellular and Molecular Life Sciences*, *78*(23), 7339-7353.

Bakinowska, E., Kiełbowski, K., Boboryko, D., Bratborska, A. W., Olejnik-Wojciechowska, J., Rusiński, M., & Pawlik, A. (2024). The role of stem cells in the treatment of cardiovascular diseases. *International journal of molecular sciences*, *25*(7), 3901.

Bispo, D. S., Jesus, C. S., Marques, I. M., Romek, K. M., Oliveira, M. B., Mano, J. F., & Gil, A. M. (2021). Metabolomic applications in stem cell research: a review. *Stem cell reviews and reports*, *17*(6), 2003-2024.

Boakye Serebour, T., Cribbs, A. P., Baldwin, M. J., Masimirembwa, C., Chikwambi, Z., Kerasidou, A., & Snelling, S. J. (2024). Overcoming barriers to single-cell RNA sequencing adoption in low-and middle-income countries. *European Journal of Human Genetics*, *32*(10), 1206-1213.

Borjesson, D. L., & Overmann, J. A. (2022). Stem Cell Biology. *Schalm's Veterinary Hematology*, 9-17.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Bremers, E. K. (2026). *Characterizing a Common Mechanism of Drug Resistance in the Malaria Parasite and the Development of Metacognition in College Biology Students* University of Georgia].

Busch, C., Nyamondo, K., & Wheadon, H. (2024). Complexities of modeling the bone marrow microenvironment to facilitate hematopoietic research. *Experimental hematology*, *135*, 104233.

Casado-Díaz, A. (2022). Stem cells in regenerative medicine. In (Vol. 11, pp. 5460): MDPI.

Chen, C., Wang, J., Pan, D., Wang, X., Xu, Y., Yan, J., Wang, L., Yang, X., Yang, M., & Liu, G. P. (2023). Applications of multi-omics analysis in human diseases. *MedComm*, *4*(4), e315.

Chen, J., Su, M., Wu, X., Wu, H., Wu, H., Zhang, P., An, X., & Liu, Z. (2026). Dynamic fibrous hydrogels for stem cell homing and in situ bone regeneration. *Advanced Science*, *13*(5), e08803.

Clavellina, D., Balkan, W., & Hare, J. M. (2023). Stem cell therapy for acute myocardial infarction: Mesenchymal Stem Cells and induced Pluripotent Stem Cells. *Expert opinion on biological therapy*, *23*(10), 951-967.

Costela-Ruiz, V. J., Melguizo-Rodríguez, L., Bellotti, C., Illescas-Montes, R., Stanco, D., Arciola, C. R., & Lucarelli, E. (2022). Different sources of mesenchymal stem cells for tissue regeneration: a guide to identifying the most favorable one in orthopedics and dentistry applications. *International journal of molecular sciences*, *23*(11), 6356.

Cring, M. R., & Sheffield, V. C. (2022). Gene therapy and gene correction: targets, progress, and challenges for treating human diseases. *Gene therapy*, *29*(1), 3-12.

Dahiya, A., Singh, K., Ashish, A., Nipun, Bhadyaria, A., Thakur, S., Kumar, M., Das Gupta, G., Das Kurmi, B., & Pal, R. R. (2025). Global harmonization in advanced therapeutics: balancing innovation, safety, and access. *Personalized Medicine*, *22*(3), 181-191.

Dhaiban, S., Chandran, S., Noshi, M., & Sajini, A. A. (2025). Clinical translation of human iPSC technologies: advances, safety concerns, and future directions. *Frontiers in Cell and Developmental Biology*, *13*, 1627149.

Doxzen, K. W., Adair, J. E., Fonseca Bazzo, Y. M., Bukini, D., Cornetta, K., Dalal, V., Guerino-Cunha, R. L., Hongeng, S., Jotwani, G., & Kityo-Mutuluuza, C. (2024). The translational gap for gene therapies in low-and middle-income countries. *Science Translational Medicine*, *16*(746), eadn1902.

El-Tanani, M., Rabbani, S. A., Satyam, S. M., Rangraze, I. R., Wali, A. F., El-Tanani, Y., & Aljabali, A. A. (2025). Deciphering the role of cancer stem cells: Drivers of tumor evolution, therapeutic resistance, and precision medicine strategies. *Cancers*, *17*(3), 382.

Estrada-Meza, C., Torres-Copado, A., Loreti González-Melgoza, L., Ruiz-Manriquez, L. M., De Donato, M., Sharma, A., Pathak, S., Banerjee, A., & Paul, S. (2022). Recent insights into the microRNA and long non-coding RNA-mediated regulation of stem cell populations. *3 Biotech*, *12*(10), 270.

Farahzadi, R., Valipour, B., Montazersaheb, S., & Fathi, E. (2023). Targeting the stem cell niche micro-environment as therapeutic strategies in aging. *Frontiers in Cell and Developmental Biology*, *11*, 1162136.

Giallongo, S., Rehakova, D., Raffaele, M., Lo Re, O., Koutna, I., & Vinciguerra, M. (2021). Redox and epigenetics in human pluripotent stem cells differentiation. *Antioxidants & redox signaling*, *34*(4), 335-349.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Grace, D. (2023). Burden of foodborne disease in low-income and middle-income countries and opportunities for scaling food safety interventions. *Food Security*, *15*(6), 1475-1488.

Gulati, G. S., D'Silva, J. P., Liu, Y., Wang, L., & Newman, A. M. (2025). Profiling cell identity and tissue architecture with single-cell and spatial transcriptomics. *Nature reviews Molecular cell biology*, *26*(1), 11-31.

Han, X., Liao, R., Li, X., Zhang, C., Huo, S., Qin, L., Xiong, Y., He, T., Xiao, G., & Zhang, T. (2025). Mesenchymal stem cells in treating human diseases: molecular mechanisms and clinical studies. *Signal transduction and targeted therapy*, *10*(1), 262.

Harrell, C. R., Djonov, V., & Volarevic, V. (2021). The cross-talk between mesenchymal stem cells and immune cells in tissue repair and regeneration. *International journal of molecular sciences*, *22*(5), 2472.

He, R., Dantas, A., Riabowol, K., Allegrucci, C., & Ordóñez-Morán, P. (2021). Histone Acetyltransferases and Stem Cell Identity. *Cancers*, *13*(10).

Hoang, V. T., Nguyen, Q. T., Phan, T. T. K., Pham, T. H., Dinh, N. T. H., Anh, L. P. H., Dao, L. T. M., Bui, V. D., Dao, H. N., & Le, D. S. (2025). Tissue engineering and regenerative medicine: perspectives and challenges. *MedComm*, *6*(5), e70192.

Hu, W., & Lazar, M. A. (2022). Modelling metabolic diseases and drug response using stem cells and organoids. *Nature Reviews Endocrinology*, *18*(12), 744-759.

Huang, G., & Guo, F. (2022). Loss of life expectancy due to respiratory infectious diseases: findings from the global burden of disease study in 195 countries and territories 1990–2017. *Journal of Population Research*, *39*(1), 1-43.

Hussen, B. M., Taheri, M., Yashooa, R. K., Abdullah, G. H., Abdullah, S. R., Kheder, R. K., & Mustafa, S. A. (2024). Revolutionizing medicine: recent developments and future prospects in stem-cell therapy. *International Journal of Surgery*, *110*(12), 8002-8024.

Illi, B., & Nasi, S. (2023). Myc beyond cancer: regulation of mammalian tissue regeneration. *Pathophysiology*, *30*(3), 346-365.

Jovic, D., Liang, X., Zeng, H., Lin, L., Xu, F., & Luo, Y. (2022). Single-cell RNA sequencing technologies and applications: a brief overview. *Clinical and translational medicine*, *12*(3), e694.

Kerper, N., Ashe, S., & Hebrok, M. (2022). Pancreatic β-cell development and regeneration. *Cold Spring Harbor perspectives in biology*, *14*(5), a040741.

Kortemme, T. (2024). De novo protein design—From new structures to programmable functions. *Cell*, *187*(3), 526-544.

Kou, M., Huang, L., Yang, J., Chiang, Z., Chen, S., Liu, J., Guo, L., Zhang, X., Zhou, X., & Xu, X. (2022). Mesenchymal stem cell-derived extracellular vesicles for immunomodulation and regeneration: a next generation therapeutic tool? *Cell Death & Disease*, *13*(7), 580.

Krishnan, M., Kumar, S., Kangale, L. J., Ghigo, E., & Abnave, P. (2021). The act of controlling adult stem cell dynamics: insights from animal models. *Biomolecules*, *11*(5), 667.

Kulus, M., Sibiak, R., Stefańska, K., Zdun, M., Wieczorkiewicz, M., Piotrowska-Kempisty, H., Jaśkowski, J. M., Bukowska, D., Ratajczak, K., & Zabel, M. (2021). Mesenchymal stem/stromal cells derived from human and animal perinatal tissues—origins, characteristics, signaling pathways, and clinical trials. *Cells*, *10*(12), 3278.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Kumar, R., Johar, R., Caruso, G., Singh, M., Chandra, M., Igwegbe, C. A., Singh, D., Goyal, N., & Khandel, S. K. (2025). Pathophysiology of Alzheimer's disease: advances in drug development and therapeutic innovations. *Chemical Biology Letters*, *12*(2), 1264-1264.

Lacorazza, H. D. (2025). The reprogramming factor KLF4 in normal and malignant blood cells. *Frontiers in immunology*, *16*, 1584181.

Lee, J. Y., & Hong, S.-H. (2020). Hematopoietic stem cells and their roles in tissue regeneration. *International journal of stem cells*, *13*(1), 1-12.

Lewis, P., Silajdžić, E., Brison, D. R., & Kimber, S. J. (2020). Embryonic stem cells. In *Cell engineering and regeneration* (pp. 315-365). Springer.

Li, J. S., Riggins, K., Yang, L., Chen, C., Castro, P., Alfarkh, W., Zarrin-Khameh, N., Scheurer, M. E., Creighton, C. J., & Musher, B. (2025). DNA methylation profiling at base-pair resolution reveals unique epigenetic features of early-onset colorectal cancer in underrepresented populations. *Clinical Epigenetics*, *17*(1), 11.

Li, P., Ou, Q., Shi, S., & Shao, C. (2023). Immunomodulatory properties of mesenchymal stem cells/dental stem cells and their therapeutic applications. *Cellular & molecular immunology*, *20*(6), 558-569.

Li, S.-w., Cai, Y., Mao, X.-l., He, S.-q., Chen, Y.-h., Yan, L.-l., Zhou, J.-j., Song, Y.-q., Ye, L.-p., & Zhou, X.-b. (2021). The immunomodulatory properties of mesenchymal stem cells play a critical role in inducing immune tolerance after liver transplantation. *Stem Cells International*, *2021*(1), 6930263.

Liu, G., David, B. T., Trawczynski, M., & Fessler, R. G. (2020). Advances in pluripotent stem cells: history, mechanisms, technologies, and applications. *Stem cell reviews and reports*, *16*(1), 3-32.

Liu, G., Lin, Q., Jin, S., & Gao, C. (2022). The CRISPR-Cas toolbox and gene editing technologies. *Molecular cell*, *82*(2), 333-347.

Lopes, M. B., Coletti, R., Duranton, F., Glorieux, G., Jaimes Campos, M. A., Klein, J., Ley, M., Perco, P., Sampri, A., & Tur-Sinai, A. (2025). The omics-driven machine learning path to cost-effective precision medicine in chronic kidney disease. *Proteomics*, *25*(11-12), e202400108.

Loukelis, K., Koutsomarkos, N., Mikos, A. G., & Chatzinikolaidou, M. (2024). Advances in 3D bioprinting for regenerative medicine applications. *Regenerative biomaterials*, *11*, rbae033.

Luce, E., & Jean-Charles, D.-V. (2025). Stem cells and organoids: A paradigm shift in preclinical models toward personalized medicine. *Pharmaceuticals*, *18*(7), 992.

Ma, H., Qu, J., Pang, Z., Luo, J., Yan, M., Xu, W., Zhuang, H., Liu, L., & Qu, Q. (2024). Super-enhancer omics in stem cell. *Molecular Cancer*, *23*(1), 153.

Maldonado, V. V., Patel, N. H., Smith, E. E., Barnes, C. L., Gustafson, M. P., Rao, R. R., & Samsonraj, R. M. (2023). Clinical utility of mesenchymal stem/stromal cells in regenerative medicine and cellular therapy. *Journal of biological engineering*, *17*(1), 44.

Mannino, G., Russo, C., Maugeri, G., Musumeci, G., Vicario, N., Tibullo, D., Giuffrida, R., Parenti, R., & Lo Furno, D. (2022). Adult stem cell niches for tissue homeostasis. *Journal of Cellular Physiology*, *237*(1), 239-257.

Mao, J., Saiding, Q., Qian, S., Liu, Z., Zhao, B., Zhao, Q., Lu, B., Mao, X., Zhang, L., & Zhang, Y. (2022). Reprogramming stem cells in regenerative medicine. *Smart Medicine*, *1*(1), e20220005.

Maraldi, T., & Russo, V. (2022). Amniotic fluid and placental membranes as sources of stem cells: progress and challenges. *International journal of molecular sciences*, *23*(10), 5362.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Marchal, I. (2025). Making cell therapy accessible: challenges and opportunities. *nature biotechnology*, *43*(4), 482-486.

Marei, H. E. (2025). Stem cell therapy: a revolutionary cure or a pandora's box. *Stem Cell Research & Therapy*, *16*(1), 255.

McKinley, K. L., Longaker, M. T., & Naik, S. (2023). Emerging frontiers in regenerative medicine. *Science*, *380*(6647), 796-798.

Meir, Y.-J. J., & Li, G. (2021). Somatic Reprogramming—Above and beyond pluripotency. *Cells*, *10*(11), 2888.

Merkle, F. T., Ghosh, S., Genovese, G., Handsaker, R. E., Kashin, S., Meyer, D., Karczewski, K. J., O'Dushlaine, C., Pato, C., & Pato, M. (2022). Whole-genome analysis of human embryonic stem cells enables rational line selection based on genetic variation. *Cell stem cell*, *29*(3), 472-486. e477.

Mihai, M. C., Popa, M. A., Şuică, V. I., Antohe, F., Jackson, E. K., Leeners, B., Simionescu, M., & Dubey, R. K. (2021). Proteomic analysis of estrogen-mediated enhancement of mesenchymal stem cell-induced angiogenesis in vivo. *Cells*, *10*(9), 2181.

Moreno, V., Thistlethwaite, F., Yarza, R., Tak, W. S., Lim, K. H. J., & Haanen, J. B. (2026). Advances in cell therapy for solid tumours: European perspective and future directions. *The Lancet Regional Health–Europe*, *64*.

Morganti, C., Cabezas-Wallscheid, N., & Ito, K. (2022). Metabolic regulation of hematopoietic stem cells. *Hemasphere*, *6*(7), e740.

Mukherjee, A. (2025). Revolutionizing cancer care in India: pioneering low-cost, next-generation CAR-T cell therapies to position India as a global leader in precision oncology. *Proceedings of the Indian National Science Academy*, 1-27.

Na, J., Tai, C., Wang, Z., Yang, Z., Chen, X., Zhang, J., Zheng, L., & Fan, Y. (2025). Stiff extracellular matrix drives the differentiation of mesenchymal stem cells toward osteogenesis by the multiscale 3D genome reorganization. *Biomaterials*, *312*, 122715.

Niu, C., Wang, S., Guo, J., Wei, X., Jia, M., Chen, Z., Gong, W., Qin, Y., Wang, X., & Zhi, X. (2021). BACH1 recruits NANOG and histone H3 lysine 4 methyltransferase MLL/SET1 complexes to regulate enhancer–promoter activity and maintains pluripotency. *Nucleic acids research*, *49*(4), 1972-1986.

Ogbogu, U., & Albrecht, L. (2025). Toward Epistemic Justice: Regenerative Medicine Activity and Governance. *Regenerative Medicine and the Bioethics of Globalization, Justice and Hegemony*, 17.

Ogbogu, U., & Albrecht, L. (2026). Toward Epistemic Justice: Regenerative Medicine Activity and Governance in Low-and Middle-Income Countries. In *Regenerative Medicine and the Bioethics of Globalization, Justice and Hegemony* (pp. 17-42). Springer.

Ogi, D. A., & Jin, S. (2023). Transcriptome-powered pluripotent stem cell differentiation for regenerative medicine. *Cells*, *12*(10), 1442.

Pal, D., Das, P., Roy, S., Mukherjee, P., Halder, S., Ghosh, D., & Nandi, S. K. (2024). Recent trends of stem cell therapies in the management of orthopedic surgical challenges. *International Journal of Surgery*, *110*(10), 6330-6344.

Palasantzas, V. E., Tamargo-Rubio, I., Le, K., Slager, J., Wijmenga, C., Jonkers, I. H., Kumar, V., Fu, J., & Withoff, S. (2023). iPSC-derived organ-on-a-chip models for personalized human genetics and pharmacogenomics studies. *Trends in Genetics*, *39*(4), 268-284.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Park, J., Kim, J., Shin, B., Schöler, H. R., Kim, J., & Kim, K.-P. (2024). Inducing pluripotency in somatic cells: historical perspective and recent advances. *International journal of stem cells*, *17*(4), 363-373.

Parvatam, S., Pistollato, F., Marshall, L. J., Furtmann, F., Jahagirdar, D., Chakraborty Choudhury, M., Mohanty, S., Mittal, H., Meganathan, S., & Mishra, R. (2025). Human-based complex in vitro models: their promise and potential for rare disease therapeutics. *Frontiers in Cell and Developmental Biology*, *13*, 1526306.

Poliwoda, S., Noor, N., Downs, E., Schaaf, A., Cantwell, A., Ganti, L., Kaye, A. D., Mosel, L. I., Carroll, C. B., & Viswanath, O. (2022). Stem cells: a comprehensive review of origins and emerging clinical roles in medical practice. *Orthopedic reviews*, *14*(3), 37498.

Rahimi Darehbagh, R., Seyedoshohadaei, S. A., Ramezani, R., & Rezaei, N. (2024). Stem cell therapies for neurological disorders: current progress, challenges, and future perspectives. *European Journal of Medical Research*, *29*(1), 386.

Rajalekshmi, R., & Agrawal, D. K. (2025). Synergistic potential of stem cells and microfluidics in regenerative medicine. *Molecular and Cellular Biochemistry*, *480*(3), 1481-1493.

Rasekh, M., Arshad, M. S., & Ahmad, Z. (2025). Advances in drug delivery integrated with regenerative medicine: innovations, challenges, and future frontiers. *Pharmaceutics*, *17*(4), 456.

Rasool, S., Hussain, A., Mushtaq, A., Asghar, S., & Arshad, R. (2026). EXOME ENGINEERING IN PRECISION MEDICINE: CRISPR-BASED THERAPEUTIC STRATEGIES FOR GENETIC DISEASES AND CANCER. *Review Journal of Neurological & Medical Sciences Review*, *4*(6), 347-354. https://doi.org/10.63075/26x5wk50

Ray-Jones, H., & Spivakov, M. (2021). Transcriptional enhancers and their communication with gene promoters. *Cellular and Molecular Life Sciences*, *78*(19-20), 6453-6485.

Ren, H., Jia, X., & Yu, L. (2025). The building blocks of embryo models: embryonic and extraembryonic stem cells. *Cell Discovery*, *11*(1), 40.

Riveiro, A. R., & Brickman, J. M. (2020). From pluripotency to totipotency: an experimentalist's guide to cellular potency. *Development*, *147*(16), dev189845.

Rosner, M., Horer, S., Feichtinger, M., & Hengstschläger, M. (2023). Multipotent fetal stem cells in reproductive biology research. *Stem Cell Research & Therapy*, *14*(1), 157.

Rouce, R. H., & Grilley, B. J. (2025). How to democratize cell and gene therapy: a global approach. *Molecular Therapy*, *33*(5), 2082-2090.

Russa, A. D., & Mtebe, M. M. (2026). Integrating Regenerative Medicine into Medical Curricula in the Global South: A Tanzanian Perspective. In *Regenerative Medicine and the Bioethics of Globalization, Justice and Hegemony* (pp. 61-77). Springer.

Ruta, A., Krishnan, K., & Elisseeff, J. H. (2024). Single-cell transcriptomics in tissue engineering and regenerative medicine. *Nature Reviews Bioengineering*, *2*(2), 101-119.

Saba, J. A., Liakath-Ali, K., Green, R., & Watt, F. M. (2021). Translational control of stem cell function. *Nature reviews Molecular cell biology*, *22*(10), 671-690.

Sadeghi, M., Moghaddam, A., Amiri, A. M., Charoghdoozi, K., Mohammadi, M., Dehnavi, S., & Orazizadeh, M. (2025). Improving the wound healing process: pivotal role of mesenchymal stromal/stem cells and immune cells. *Stem cell reviews and reports*, *21*(3), 680-697.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Salybekov, A. A., Wolfien, M., Kobayashi, S., Steinhoff, G., & Asahara, T. (2021). Personalized cell therapy for patients with peripheral arterial diseases in the context of genetic alterations: artificial intelligence-based responder and non-responder prediction. *Cells*, *10*(12), 3266.

Semba, T., Sammons, R., Wang, X., Xie, X., Dalby, K. N., & Ueno, N. T. (2020). JNK signaling in stem cell self-renewal and differentiation. *International journal of molecular sciences*, *21*(7), 2613.

Shah, A. A., & Khan, F. A. (2021). Types and classification of stem cells. In *Advances in application of stem cells: From Bench to Clinics* (pp. 25-49). Springer.

Silva-Sousa, T., Nakanishi Usuda, J., Al-Arawe, N., Hinterseher, I., Catar, R., Luecht, C., Vallecillo Garcia, P., Riesner, K., Hackel, A., & Schimke, L. F. (2025). Artificial intelligence and systems biology analysis in stem cell research and therapeutics development. *Stem cells translational medicine*, *14*(10), szaf037.

Singla, N., Thapa, R., Kulshrestha, R., Bhat, A. A., Gupta, S., Purohit, M., Singh, S. K., & Gupta, G. (2023). Introduction to epigenetics. In *Targeting epigenetics in inflammatory lung diseases* (pp. 17-41). Springer.

Subhan, N. Novel Biomarkers for Early Detection of Diabetes Mellitus Complications. *International Journal of Advanced Engineering Technologies and Innovations*, *2*(1), 1-22.

Sun, W., Zheng, W., & Simeonov, A. (2017). Drug discovery and development for rare genetic disorders. *American Journal of Medical Genetics Part A*, *173*(9), 2307-2322.

Tahir, F., & Tahir, A. (2025). Regenerative medicine and stem cell therapy: advancements and future potential. *Wah Academia Journal of Health and Nutrition*, *1*(1), 19-30.

Tang, X.-Y., Wu, S., Wang, D., Chu, C., Hong, Y., Tao, M., Hu, H., Xu, M., Guo, X., & Liu, Y. (2022). Human organoids in basic research and clinical applications. *Signal transduction and targeted therapy*, *7*(1), 168.

Tedesco, M., Giannese, F., Lazarević, D., Giansanti, V., Rosano, D., Monzani, S., Catalano, I., Grassi, E., Zanella, E. R., & Botrugno, O. A. (2022). Chromatin Velocity reveals epigenetic dynamics by single-cell profiling of heterochromatin and euchromatin. *nature biotechnology*, *40*(2), 235-244.

Theodorakis, N., Feretzakis, G., Tzelves, L., Paxinou, E., Hitas, C., Vamvakou, G., Verykios, V. S., & Nikolaou, M. (2024). Integrating machine learning with multi-omics technologies in geroscience: towards personalized medicine. *Journal of personalized medicine*, *14*(9), 931.

Trapana, J., Weinerman, J., Lee, D., Sedani, A., Constantinescu, D., Best, T. M., Hornicek Jr, F. J., & Hare, J. M. (2024). Cell-based therapy in the treatment of musculoskeletal diseases. *Stem cells translational medicine*, *13*(10), 959-978.

Tsai, I., & Sun, C.-K. (2024). Stem cell therapy against ischemic heart disease. *International journal of molecular sciences*, *25*(7), 3778.

Turner, E., White, C., & Thompson, D. (2025). Commercialization Challenges in Regenerative Medicine.

Uversky, V. N., & Giuliani, A. (2021). Networks of networks: an essay on multi-level biological organization. *Frontiers in genetics*, *12*, 706260.

Valdés, E., & Lecaros, J. A. (2024). Biobanks and data interoperability in Latin America: Engendering high-quality evidence for the global research ecosystem. *Frontiers in medicine*, *11*, 1481891.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Varzideh, F., Gambardella, J., Kansakar, U., Jankauskas, S. S., & Santulli, G. (2023). Molecular mechanisms underlying pluripotency and self-renewal of embryonic stem cells. *International journal of molecular sciences*, *24*(9), 8386.

Vitorino, R. (2024). Transforming clinical research: the power of high-throughput omics integration. *Proteomes*, *12*(3), 25.

Wang, J. Y., & Doudna, J. A. (2023). CRISPR technology: A decade of genome editing is only the beginning. *Science*, *379*(6629), eadd8643.

Wang, M., & Du, L. (2026). Regenerative Medicine in China: Current Regulatory Challenges and Global Advancements. In *Regenerative Medicine and the Bioethics of Globalization, Justice and Hegemony* (pp. 183-256). Springer.

Wang, X., Gao, M., Wang, Y., & Zhang, Y. (2022). The progress of pluripotent stem cell-derived pancreatic β-cells regeneration for diabetic therapy. *Frontiers in endocrinology*, *13*, 927324.

Wei, L., Niraula, D., Gates, E. D., Fu, J., Luo, Y., Nyflot, M. J., Bowen, S. R., El Naqa, I. M., & Cui, S. (2023). Artificial intelligence (AI) and machine learning (ML) in precision oncology: a review on enhancing discoverability through multiomics integration. *The British journal of radiology*, *96*(1150), 20230211.

Williams, C. G., Lee, H. J., Asatsuma, T., Vento-Tormo, R., & Haque, A. (2022). An introduction to spatial transcriptomics for biomedical research. *Genome medicine*, *14*(1), 68.

Yadav, R. (2025). Clinical Application and Regulation in Stem Cells. In *Advancing Biotechnology: From Science to Therapeutics and Informatics: Technological Advancements in Biosciences and Biotechnology* (pp. 69-79). Springer.

Yamada, S., Behfar, A., & Terzic, A. (2021). Regenerative medicine clinical readiness. *Regenerative Medicine*, *16*(3), 309-322.

Yek, C., Pacheco, A. R., Vanaerschot, M., Bohl, J. A., Fahsbender, E., Aranda-Díaz, A., Lay, S., Chea, S., Oum, M. H., & Lon, C. (2022). Metagenomic pathogen sequencing in resource-scarce settings: lessons learned and the road ahead. *Frontiers in epidemiology*, *2*, 926695.

Yildirim, Z., Swanson, K., Wu, X., Zou, J., & Wu, J. (2025). Next-gen therapeutics: pioneering drug discovery with iPSCs, genomics, AI, and clinical trials in a dish. *Annual review of pharmacology and toxicology*, *65*(1), 71-90.

Yiu, T., Chen, B., Wang, H., Feng, G., Fu, Q., & Hu, H. (2025). Transformative advances in single-cell omics: a comprehensive review of foundation models, multimodal integration and computational ecosystems. *Journal of Translational Medicine*, *23*(1), 1176.

Yushkov, B., Chereshnev, V., Korneva, E., Yushkova, V., & Sarapultsev, A. (2025). Stem-cell niches in health and disease: microenvironmental determinants of regeneration and pathology. *Cells*, *14*(13), 981.

Zayed, M., Massoud, A., Al-Haddad, R., Al-Kubaisi, A., Said, W., Atiaa, A., & Jeong, B.-H. (2026). Integrating Single-Cell Sequencing and Proteomics to Unravel Stem Cell Heterogeneity: Implications for Precision Regenerative Medicine. *Stem cell reviews and reports*, 1-23.

Zeng, L., Yu, G., Yang, K., Wang, X., Li, J., & Chen, H. (2022). Efficacy and safety of mesenchymal stem cell transplantation in the treatment of autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, multiple sclerosis, and ankylosing spondylitis): a systematic review and meta-analysis of randomized controlled trial. *Stem Cells International*, *2022*.

Zgeib, K. (2025). *Molecular Characterization of Dedifferentiation-Induced Oncogenic Stemness in the Intestinal Epithelium* Stevens Institute of Technology].

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Zhao, X., Li, Q., Guo, Z., & Li, Z. (2021). Constructing a cell microenvironment with biomaterial scaffolds for stem cell therapy. *Stem Cell Research & Therapy*, *12*(1), 583.

Zhao, Z., Chen, X., Dowbaj, A. M., Sljukic, A., Bratlie, K., Lin, L., Fong, E. L. S., Balachander, G. M., Chen, Z., & Soragni, A. (2022). Organoids. *Nature Reviews Methods Primers*, *2*(1), 94.

Zhao, Z., Shang, P., Mohanraju, P., & Geijsen, N. (2023). Prime editing: advances and therapeutic applications. *Trends in Biotechnology*, *41*(8), 1000-1012.

Zhou, H., Ye, P., Xiong, W., Duan, X., Jing, S., He, Y., Zeng, Z., Wei, Y., & Ye, Q. (2024). Genome-scale CRISPR-Cas9 screening in stem cells: theories, applications and challenges. *Stem Cell Research & Therapy*, *15*(1), 218.

Zhou, Q., Zhao, Z., Tan, D., Fang, C., Shen, Z., Li, S., & Chen, X. (2026). Multi-omics technologies: Novel tools and methods for assessing nerve injury and regeneration. *Neural Regeneration Research*, *21*(9), 4051-4060.

Zhu, Z., Wu, X., Li, Q., Zhang, J., Yu, S., Shen, Q., Zhou, Z., Pan, Q., Yue, W., & Qin, D. (2021). Histone demethylase complexes KDM3A and KDM3B cooperate with OCT4/SOX2 to define a pluripotency gene regulatory network. *The FASEB Journal*, *35*(6), e21664.