Crimson Publishers
Wings to the Research

Mini Review

Unlocking the Potential: A Concise Exploration of Stem Cell Biology and Differentiation

Muhammad Umar Sharif[1]*, Shah Nawaz[1], Tahira Iftakhar[2] and Hafiz Muhammad Aslam[3]

[1]Department of Anatomy, Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan

[2]College of Animal science and Technology, Huazhong Agriculture University Wuhan, Hubei, China

[3]Department of Biochemistry, University of Agriculture Faisalabad, Pakistan

ISSN: 2578-0204

***Corresponding author:** Muhammad Umar Sharif, Department of Anatomy, Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan

Submission: November 14, 2023

Published: January 05, 2024

Volume 4 - Issue 3

How to cite this article: Muhammad Umar Sharif*, Shah Nawaz, Tahira Iftakhar and Hafiz Muhammad Aslam. Unlocking the Potential: A Concise Exploration of Stem Cell Biology and Differentiation. Open J Cardiol Heart Dis. 4(3). OJCHD.000588. 2024.
DOI: 10.31031/OJCHD.2024.04.000588

Abstract

Stem cells, with their remarkable potential for self-renewal and differentiation into diverse specialized cell types, constitute a central focus in scientific research and medical exploration. This review delves into the intricate realm of stem cell biology, spotlighting the processes of cell differentiation and development. Stem cells, spanning embryonic, adult, and induced pluripotent varieties, offer unparalleled insights into early embryonic development, and bear the promise of revolutionizing regenerative medicine and disease modeling. The journey of stem cell differentiation, governed by intricate mechanisms, entails signal transduction pathways, gene expression regulation, epigenetic modifications, niche interactions, and asymmetric cell division, culminating in cell fate commitment and lineage-specific maturation. Stem cells play a pivotal role in embryonic development, giving rise to the gamut of tissue-specific cell types, and hold substantial potential in regenerative medicine, disease modeling, and drug discovery. Yet, persistent challenges and ethical dilemmas envelop the field, spanning concerns over embryonic stem cell use, reprogramming techniques, tumor formation, immune rejection, and regulatory complexities. As the field advances, the collaborative endeavors of multidisciplinary teams drive emerging trends, technologies, and potential breakthroughs, offering a glimpse into a future where stem cells may redefine healthcare. The resolution of these challenges and ethical considerations is instrumental in advancing the ethical and responsible application of stem cells in both research and clinical contexts.

Keywords: Stem cells; Biology; IPSCs; Regenerative medicine; Cell differentiation; Tissue engineering

Introduction

Stem cells (SCs) are fundamental for tissue development and maintenance and are defined by their ability to self-renew and differentiate into various cell lineages [1]. They serve as a repair mechanism within living organisms [2], playing a vital role in the growth and development of multicellular organisms and maintaining cellular homeostasis [3]. These versatile cells are central to developing treatments for tissue-specific diseases and injuries [4] and have significant potential in regenerative medicine for replacing damaged cells, tissues, and organs [5]. Additionally, SCs are invaluable tools for investigating fundamental biological processes like cell differentiation, tissue development, and organogenesis [6]. Now a days, SCs are at the forefront of scientific and medical research that has potential to transform our understanding of development, regeneration, and disease [7]. SCs, whether embryonic, adult, or induced pluripotent, hold the capacity to generate diverse cell types, pivotal in both normal physiology and disease treatment [8]. Understanding to the SC differentiation is essential for unravelling early embryonic development intricacies and harnessing their therapeutic potential [6,9]. This review covers stem cell classification, molecular mechanisms, and applications in regenerative medicine, as well as ethical considerations and future directions in this evolving field which could provide basics for preclinical studies.

Properties and classification of SCs

SCs, unlike limited-division progenitor cells, exhibit lifelong cell division potential. While the body has numerous cells, they may not effectively repair damaged or compromised tissue, emphasizing the importance of regenerative medicine, particularly in injuries [10]. Hence, SCs are undifferentiated cells with the potential to give rise to all mature cell types in the body. They undergo either symmetric division, producing identical cells like cloning, or asymmetric division, resulting in cells that can differentiate into various cell types. SCs predominantly follow asymmetric division, ensuring their ability to self-renew and differentiate [11-14]. These cells exhibit three key attributes: proliferation, differentiation, and stemness [15]. Proliferation involves cell division while retaining an undifferentiated state, with the potential to transform into specialized cell types under specific conditions [16]. Stemness describes the ability of cells to maintain its lineage, working in coordination with its microenvironment (niche) to balance between growth, dormancy, and renewal, ensuring a dynamic equilibrium [15,17,18].

The body of an organism contains about 220 sorts of cells that are very specific in their function, but all the specialized cells are derived from the unspecialized cells via differentiation [9,19]. Researchers have different classification criteria for stem cells, with some categorizing them based on their source, distinguishing between embryonic and non-embryonic stem cells [20], while others classify them according to their differentiation potential. Both approaches offer valid ways to classify stem cells, allowing for flexibility in nomenclature [21,22]. However, SCs are classified either based on cellular potency or origin [23]. They can be divided into one of the following groups as totipotent, pluripotent, multipotent, oligopotent, and unipotent. Totipotent cells, like zygotes, can develop into any cell type, even forming a complete organism [24]. Pluripotent cells, exemplified by embryonic stem cells, have broader differentiation potential but can't create an entire organism. Multipotent cells, such as hematopoietic stem cells in the bone marrow, differentiate into a range of related cell types. Oligopotent cells, like myeloid stem cells, are more specialized and only differentiate into a few related cell types. Unipotent cells, such as muscle satellite cells, are highly specialized and only become a single cell type, like muscle cells [25,26]. While based on origin, they can be classified as embryonic stem cells (early), and adult stem cells (mature). Embryonic stem cells (ESCs), derived from the inner cell mass of the blastomere, are pluripotent cells capable of generating all three germinal layers in early development. They require specific chemically defined culture conditions to maintain their undifferentiated state and are marked by surface proteins like Nanog and Oct4. Their use for research is allowed due to ethical concerns about commercial applications. In contrast, adult stem cells (ASCs), found in various adult tissues, contribute to local tissue repair and regeneration. While the exact origin of ASCs is not fully understood, they can be isolated from tissues like bone marrow, liver, skin, and others, and they retain their stemness for future use in healing and growth [23,27].

However, induced pluripotent stem cells (iPSCs) represent another distinct category of SCs, characterized by their origin as reprogrammed adult cells. iPSCs are created by introducing specific genes into adult cells, returning them to a pluripotent state, like ESCs. This reprogramming technique was first pioneered by Shinya Yamanaka's groundbreaking work in 2006 [28]. By reprogramming somatic cells like skin fibroblasts or blood cells into iPSCs, researchers have unlocked the potential to generate pluripotent stem cells from tissues of an individual, reducing issues related to immune rejection and ethical concerns associated with ESCs. iPSCs have broad implications in personalized medicine, disease modeling, and regenerative therapies, making them a remarkable innovation in the field of stem cell research [29-31].

Mechanism of cell differentiation

The mechanism of stem cell differentiation is an intricate and highly regulated process governing the transformation of pluripotent stem cells into specific, specialized cell types. This complex journey involves a series of molecular and cellular events, encompassing gene regulation, signaling pathways, and epigenetic modifications [32]. External signals, such as growth factors and hormones, initiate differentiation by binding to specific receptors on the cell surface, triggering intracellular signaling pathways. These pathways, including Wnt, Notch, and TGF-β, drive changes in gene expression and cellular behavior [33,34]. Central to this process, there are certain key transcription factors and regulatory genes that turn other genes on or off, steering the cell toward a particular lineage. Transcription factors like Oct4, Sox2, and Nanog maintain pluripotency, while lineage-specific transcription factors propel differentiation [35].

Epigenetic changes, including DNA methylation and histone modifications, impact gene expression and are vital for differentiation [36]. As SCs differentiate, specific genes become epigenetically marked, either activating or repressing them, contributing to the stability of cells in its chosen lineage [37]. Furthermore, the specialized environment within tissues, known as the niche, plays a crucial role in directing differentiation by providing physical and chemical cues, extracellular matrix proteins, and interaction with neighboring cells. SCs can also respond to mechanical forces, oxygen levels, and local chemical gradients within their niches. During cell division, SCs often undergo asymmetric division, generating one daughter cell committed to differentiation while the other maintains its stem cell identity for self-renewal. The orientation of the division plane and the distribution of cellular components influence the fate of the daughter cells [12,14,36,38].

Multiple feedback loops and cross-regulatory mechanisms are in place to fine-tune the differentiation processes, ensuring a balance between self-renewal and differentiation, which is essential for maintaining tissue composition [32]. As differentiation progresses, SCs gradually commit to a particular lineage, leading to a progressive restriction of their potential and increasing limitations in differentiation options. Even after committing to a lineage, the process continues through successive stages of maturation, with cells acquiring specific functional characteristics and morphology until they become fully specialized. This intricate process underpins the remarkable capabilities of SCs and plays a pivotal role in regenerative medicine and our understanding of developmental biology [10,11].

Applications of stem cells in development

SCs are pivotal in the formation of multicellular organisms during embryonic development [9]. ESCs possess pluripotency, generating the three primary germ layers (ectoderm, mesoderm, and endoderm) from which all tissues and organs originate [39]. By unlocking the secrets of ESCs differentiation, scientists can understand embryogenesis and can reverse the developmental anomaly [40]. SCs hold great promise in regenerative medicine, mending damaged tissues in conditions like cardiac diseases and neurodegenerative disorders [5]. They revolutionize disease modeling and drug testing by reprogramming somatic cells into iPSCs and differentiating them into affected cell types, offering insights into disease mechanisms and accelerating drug development [30]. Recent advancements in gene editing, 3D bioprinting, and our understanding of signaling pathways and epigenetic regulation have enriched contemporary stem cell research, advancing our comprehension of development and its applications [35,37].

Challenges and ethical considerations

Stem cell research holds enormous promise but also grapples with a complex web of challenges and ethical considerations such as ethical dilemmas, technical hurdles, and divergent international regulations [41]. Ethical dilemmas, including the use of human ESCs and the creation of chimeras, have led to varying international regulations. Technical hurdles involve the risk of teratoma formation, immune rejection, and the efficiency of reprogramming cells into iPSCs [42].

Divergent international regulations present a barrier to global collaboration, and the commercialization of stem cell-based therapies raises concerns about intellectual property and accessibility. Regulatory agencies must establish robust evaluation frameworks. To address these issues, strategies include ethical oversight committees, international collaboration, patient and public engagement, and ensuring transparency in research and clinical trials, ultimately maintaining the highest ethical standards in stem cell research [11,43,44].

Future directions in stem cell research

Stem cell research is an ever-evolving field, offering exciting prospects for the future. The field of stem cell research is witnessing rapid advancements in various emerging trends and technologies. High-throughput single-cell analysis techniques are providing scientists with the tools to delve deeper into the intricacies of stem cell populations and their differentiation dynamics, enhancing our understanding of these processes [45].

Furthermore, precise genome editing techniques, such as CRISPR/Cas9, continue to evolve, empowering researchers to manipulate SCs for both therapeutic purposes and fundamental research [46]. The development of complex three-dimensional organoids derived from SCs is revolutionizing the study of development, diseases, and drug screening by more accurately replicating the tissue microenvironment [47,48]. In addition, the integration of artificial intelligence and computational biology is proving invaluable in analyzing the vast amounts of data generated in stem cell research, facilitating the identification of critical factors in differentiation and development, ultimately propelling the field forward [45,49].

Exciting prospects abound in stem cell research, with several promising areas and potential breakthroughs on the horizon. Personalized medicine stands to benefit significantly from patient-specific iPSCs, offering the potential for tailored disease modeling and therapies, thereby enhancing our understanding of genetic disorders [49,50]. Stem cell-based therapies for neurological conditions, such as Alzheimer's, Parkinson's, and spinal cord injuries, represent a high-impact research avenue with the potential for transformative breakthroughs in patient care [48,51]. Moreover, SCs may contribute to advancing regenerative agriculture, offering opportunities for sustainable and animal-free meat and plant-based food production [52]. Advancements in tissue engineering and organoid development hold the promise of creating functional artificial organs, addressing the persistent shortage of donor organs available for transplantation, and opening new frontiers in regenerative medicine and agriculture [47,53,54]. The translation of stem cell-based therapies into clinical trials continues to be a prominent trend in the field, with a particular emphasis on evaluating safety and efficacy in treating conditions such as heart disease, diabetes, and blindness [55,56].

Furthermore, applications of SCs in regenerative medicine are poised to broaden their scope, encompassing a wider range of diseases and injuries, including cartilage repair, bone regeneration, and wound healing [56-58]. Innovations in immunomodulation techniques are expected to play a pivotal role in addressing the challenge of immune rejection in stem cell transplantation, offering significant potential to enhance the success and reach of stem cell therapies in clinical settings [45,55].

The importance of interdisciplinary collaboration in stem cell research cannot be overstated [59]. To confront the intricate challenges spanning from laboratory discoveries to clinical translation, the integration of expertise across diverse fields such as biology, clinical practice, engineering, computational science, and bioethics is imperative [60]. Collaborative efforts are essential not only for the advancement of scientific knowledge but also for the development of robust ethical frameworks and responsible policies that guide stem cell research and clinical applications [61]. Moreover, the sharing of data and the standardization of methods and protocols in a collaborative manner will contribute significantly to enhancing the reproducibility and comparability of stem cell research on a global scale, fostering more efficient and effective progress in the field [59,62].

Conclusion

The intricate world of stem cell biology, focusing on cell differentiation and development, unfolds as a promising frontier in science and medicine. Stem cells, spanning various types, hold the potential to revolutionize healthcare, offering personalized treatments, novel disease models, and tissue engineering possibilities. While ethical dilemmas and technical challenges persist but interdisciplinary collaboration and international cooperation can pave the way for ethical, effective, and safe applications. However, the persistent gap in understanding and addressing the ethical and technical challenges underscores the need for ongoing research, ethical oversight, and innovative solutions. The future, marked by emerging technologies and promising research domains, ensures that the journey of stem cells from pluripotency to specialization remains an ever-evolving, transformative narrative in the realms of biology, medicine, and human well-being.

References

1. Martinez P, Ballarin L, Ereskovsky AV, Gazave E, Hobmayer B, et al. (2022) Articulating the "stem cell niche" paradigm through the lens of non-model aquatic invertebrates. BMC Biology 20(1): 23.
2. McCulloch EA, Till JE (2005) Perspectives on the properties of stem cells. Nature Medicine 11(10): 1026-1028.
3. Blau HM, Brazelton T, Weimann J (2001) The evolving concept of a stem cell: entity or function? Cell 105(7): 829-841.
4. Clevers H (2016) Modeling development and disease with organoids. Cell 165(7): 1586-1597.
5. Yalcinkaya TM, Sittadjody S, Opara EC (2014) Scientific principles of regenerative medicine and their application in the female reproductive system. Maturitas 77(1): 12-19.
6. Li N, Liangyu M, Zhang G, Zhang L, Zhang N, et al. (2020) Synovial membrane mesenchymal stem cells: Past life, current situation, and application in bone and joint diseases. J Stem Cell Research and Therapy 11(1): 1-12.
7. Weber AE, Bolia IK, Trasolini NA (2021) Biological strategies for osteoarthritis: From early diagnosis to treatment. International Orthopaedics 45(2): 335-344.
8. Sarkar A, Saha S, Paul A, Maji A, Roy P, et al. (2021) Understanding stem cells and its pivotal role in regenerative medicine. Life Sciences 273: 119270.
9. Sidhu KS (2012) Frontiers in pluripotent stem cells research and therapeutic potentials bench-to-bedside. Bentham Science Publishers 9: 61-78.
10. Castro JC, Wang D, Chien GCC (2019) Regenerative Medicine. In: Abd-Elsayed A (Ed.), Pain: A Review Guide, Springer International Publishing, Berlin, Germany, pp. 1095-1098.
11. Charitos IA, Ballini A, Cantore S, Boccellino M, Di Domenico M, et al. (2021) Stem cells: a historical review about biological, religious, and ethical issues. Stem Cells International 2021: 1-11.
12. Yamashita YM (2010) Cell adhesion in regulation of asymmetric stem cell division. Current Opinion in Cell Biology 22(5): 605-610.
13. Nam Y, Rim YA, Lee J, Ju JH (2018) Current therapeutic strategies for stem cell-based cartilage regeneration. Stem Cells International 2018: 8490489.
14. Morrison SJ, Kimble J (2006) Asymmetric and symmetric stem-cell divisions in development and cancer. Nature 441(7097): 1068-1074.
15. Nazbar A, Samani S, Kashani SY, Amanzadeh A, Shoeibi S, et al. (2022) Molecular imprinting as a simple way for the long-term maintenance of the stemness and proliferation potential of adipose-derived stem cells: an in vitro study. Journal of Materials Chemistry B 10(35): 6816-6830.
16. Hemeryck L, Hermans F, Chappell J, Kobayashi H, Lambrechts D, et al. (2022) Organoids from human tooth showing epithelial stemness phenotype and differentiation potential. Cellular and Molecular Life Sciences 79(3): 153.
17. Sistigu A, Musella M, Galassi C, Vitale I, De Maria R, et al. (2020) Tuning cancer fate: tumor microenvironment's role in cancer stem cell quiescence and reawakening. Frontiers in Immunology 11: 2166.
18. Aponte PM, Caicedo A (2017) Stemness in cancer: Stem cells, cancer stem cells, and their microenvironment. Stem Cells International 2017: 5619472.
19. Scott MA, Nguyen VT, Levi B, James AW (2011) Current methods of adipogenic differentiation of mesenchymal stem cells. Stem Cells Development 20(10): 1793-1804.
20. Bongso A, Lee EH (2005) Stem cells: Their definition, classification and sources. Stem Cells, pp. 1-13.
21. Laplane L, Solary E (2019) Towards a classification of stem cells. Elife 8: e46563.
22. Gao Q, Wang L, Wang S, Huang B, Jing Y, et al. (2022) Bone marrow mesenchymal stromal cells: Identification, classification, and differentiation. Frontiers in Cell and Developmental Biology 9: 787118.
23. Zakrzewski W, Dobrzyński M, Szymonowicz M, Rybak Z (2019) Stem cells: past, present, and future. Stem Cell Research and Therapy 10(1): 68.
24. Baker CL, Pera MF (2018) Capturing totipotent stem cells. Cell Stem Cell 22(1): 25-34.
25. Bacakova L, Zarubova J, Travnickova M, Musilkova J, Pajorova J, et al. (2018) Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells-a review. Biotechnology Advances 36(4): 1111-1126.
26. Rajabzadeh N, Fathi E, Farahzadi R (2019) Stem cell-based regenerative medicine. Stem Cell Investigation 6: 19.
27. Shah AA, Khan FA (2021) Types and classification of stem cells 2021: 25-49.
28. Takahashi K, Yamanaka S (2006) Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126(4): 663-676.
29. Kalra K, Tomar PC (2014) Stem cell: basics, classification and applications. Phytomedicine and Clinical Therapeutics 2(7): 919-930.
30. Huang CY, Liu CL, Ting CY, Chiu YT, Cheng YC, et al. (2019) Human iPSC banking: Barriers and opportunities. Journal of Biomedical Science 26(1): 87.
31. Zeng H, Zeng RL, Fu W, Ji WH, Lan DL (2023) Research progress in the application and establishment of bovine induced pluripotent stem cells. Biotechnology Bulletin 39(5): 130-141.
32. Zhang K, Yang X, Zhao Q, Li Z, Fu F, et al. (2020) Molecular mechanism of stem cell differentiation into adipocytes and adipocyte differentiation of malignant tumor. Stem Cells International 2020: 8892300.
33. Luo K (2017) Signaling cross talk between TGF-β/Smad and other signaling pathways. Cold Spring Harbor Perspectives in Biology 9(1): a022137.
34. Zhang Q, Pan Y, Ji J, Xu Y, Zhang Q, et al. (2021) Roles and action mechanisms of WNT4 in cell differentiation and human diseases: A review. Cell Death Discovery 7(1): 287.
35. Swain N, Thakur M, Pathak J, Swain B (2020) SOX_2, OCT_4 and NANOG: The core embryonic stem cell pluripotency regulators in oral carcinogenesis. Journal Of Oral and Maxillofacial Pathology 24(2): 368-373.
36. Im GI, TK Kim (2020) Regenerative therapy for osteoarthritis: A perspective. International Journal of Stem Cells 13(2): 177-181.

37. Smith N, Shirazi S, Cakouros D, Gronthos S (2023) Impact of environmental and epigenetic changes on mesenchymal stem cells during aging. International Journal of Molecular Sciences 24(7): 6499.
38. Kubosch EJ, Lang G, Furst D, Kubosch D, Izadpanah K, et al. (2018) The potential for synovium-derived stem cells in cartilage repair. Current Stem Cell Research & Therapy 13(3): 174-184.
39. Priester C, MacDonald A, Dhar M, Bow A (2020) Examining the characteristics and applications of mesenchymal, induced pluripotent, and embryonic stem cells for tissue engineering approaches across the germ layers. Pharmaceuticals 13(11): 344.
40. Protze SI, Lee JH, Keller GM (2019) Human pluripotent stem cell-derived cardiovascular cells: from developmental biology to therapeutic applications. Cell Stem Cell 25(3): 311-327.
41. King NM, Perrin J (2014) Ethical issues in stem cell research and therapy. Stem Cell Research & Therapy 5(4): 85.
42. Omole AE, Fakoya AO, Nnawuba KC, Haider KH (2022) Common ethical considerations of human-induced pluripotent stem cell research. In: Handbook of Stem Cell Therapy, pp: 1-17.
43. Rosemann A, Vasen F, Bortz G (2019) Global diversification in medicine regulation: Insights from regenerative stem cell medicine. Science as Culture 28(2): 223-249.
44. Rosemann A (2017) Challenges to international stem cell clinical trials in countries with diverging regulations. Safety, Ethics and Regulations 2017: 301-319.
45. Mazalan M, Do TD, Zaman WS, Ramlan EI (2023) Machine learning approaches for stem cells. Current Stem Cell Reports 3: 43-56.
46. Dashtaki ME, Ghasemi S (2023) CRISPR/Cas9-based gene therapies for fighting drug resistance mediated by cancer stem cells. Current Gene Therapy 23(1): 41-50.
47. Argentati C, Tortorella I, Bazzucchi M, Morena F, Martino S (2020) Harnessing the potential of stem cells for disease modeling: progress and promises. Journal of Personalized Medicine 10(1): 8.
48. Centeno EG, Cimarosti H, Bithell A (2018) 2D versus 3D human induced pluripotent stem cell-derived cultures for neurodegenerative disease modelling. Molecular Neurodegeneration 13(1): 27.
49. MacArthur BD, Maayan A, Lemischka IR (2009) Systems biology of stem cell fate and cellular reprogramming. Nature Reviews Molecular Cell Biology 10(10): 672-681.
50. Romito A, Cobellis G (2015) Pluripotent stem cells: Current understanding and future directions. Stem Cells International 2016: 9451492.
51. Rahman MM, Islam MR, Islam MT, Harun-Or-Rashid M, Islam M, et al. (2022) Stem cell transplantation therapy and neurological disorders: Current status and future perspectives. Biology(Basel) 11(1): 147.
52. Samandari M, Saeedinejad F, Quint J, Chuah SX, Farzad R, et al. (2023) Repurposing biomedical muscle tissue engineering for cellular agriculture: challenges and opportunities. Trends in Biotechnology 41(7): 887-906.
53. Chansaenroj A, Yodmuang S, Ferreira JN (2021) Trends in salivary gland tissue engineering: From stem cells to secretome and organoid bioprinting. Tissue Engineering Part B Reviews 27(2): 155-165.
54. Markou M, Kouroupis D, Badounas F, Katsouras A, Kyrkou A, et al. (2020) Tissue engineering using vascular organoids from human pluripotent stem cell derived mural cell phenotypes. Frontiers in Bioengineering and Biotechnology 8: 278.
55. Sarsenova M, Kim Y, Raziyeva K, Kazybay B, Ogay V, et al. (2022) Recent advances to enhance the immunomodulatory potential of mesenchymal stem cells. Frontiers In Immunology 13: 1010399.
56. Zelinka A, Roelofs AJ, Kandel RA, De Bari C (2022) Cellular therapy and tissue engineering for cartilage repair. Osteoarthritis Cartilage 30(12): 1547-1560.
57. Kim YG, Choi J, Kim K (2020) Mesenchymal stem cell-derived exosomes for effective cartilage tissue repair and treatment of osteoarthritis. Biotechnol Journal 15(12): e2000082.
58. Rashid U, Sandhu MA, Yaqoob M, Yousaf A (2021) Critical bone gap repair using autologous adipose derived canine mesenchymal stem cell graft. Pakistan Veterinary Journal 41(4): 513-518.
59. Assen LS, Jongsma KR, Isasi R, Tryfonidou MA, Bredenoord AL (2022) Roles and responsibilities in stem cell research: A focus group study with stem cell researchers and patients. Regenerative Medicine 17(7): 445-459.
60. Wheatley T, Desrosiers M, Specchierla D, Lynn KE, Jackson S, et al. (2021) Increased mobility and fall reduction: An interdisciplinary approach on a hematology-oncology and stem cell transplantation unit. Clinical Journal of Oncology Nursing 25(3): 329-332.
61. Stephens N, Khan I, Errington R (2018) Analysing the role of virtualisation and visualisation on interdisciplinary knowledge exchange in stem cell research processes. Palgrave Communications 4(1): 1-13.
62. Omid-Shafiei S, Hassan M, Nüssler AK, Mustapha N, Vosough M (2023) A shadow of knowledge in stem cell science. Cell Journal 25(10): 738-740.

