SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

STEM CELL APPROACHES IN ORGAN REGENERATION AND REPAIR

Siddhesh G Waghmare, Ameetul Noor Zeba Khannam
Student at S.R.T.M.U. Nanded and Student at JNTUH, Kukatpally, Hyderabad.

Article DOI: https://doi.org/10.36713/epra18904
DOI No: 10.36713/epra18904

ABSTRACT

Recent advances in stem cell research have provided new hope for treating a variety of diseases and conditions that currently have no effective cure. Stem cells have the unique ability to differentiate into various cell types, enabling them to support tissue growth and replace damaged or specialized cells throughout the lifespan. Among the most promising types of stem cells are mesenchymal stem cells (MSCs), which are easily harvested from adipose tissue and can be cultured and expanded in the lab. Due to their versatility, MSCs have become a focal point in tissue regeneration and have been widely used in animal studies and clinical trials involving humans. This review aims to summarize the current understanding of MSCs, focusing on the various types of stem cells isolated from different animal models such as horses, pigs, goats, dogs, rabbits, cats, rats, and mice. Given the growing interest in MSCs, we will also discuss their applications in veterinary and regenerative medicine. Current research highlights the potential of MSCs in treating conditions like heart failure, wound healing, and tooth regeneration, demonstrating their broad therapeutic potential.

KEYWORDS: *Mesenchymal stem cells (MSCs), animal models, cell-based therapy, regenerative medicine*

Classification of Stem Cells

Stem cells are categorized based on their ability to differentiate into different cell types, with four primary classifications: totipotent, pluripotent, multipotent, and unipotent. These classifications reflect how many types of cells the stem cells can turn into. In addition to this, stem cells are also classified by their stage of development, which includes embryonic, fetal, infant (including umbilical cord blood), and adult stem cells.

Toti-Potent Stem Cells

Totipotent cells have the unique ability to develop into any type of cell found in the organism. In fact, they can give rise to all the cells of the body, including the three primary germ layers of the embryo (ectoderm, mesoderm, and endoderm), as well as extra-embryonic tissues like the placenta. This remarkable versatility makes totipotent cells capable of forming an entire organism from a single cell.

Pluri-Potent Stem Cells

Pluripotent stem cells are a type of stem cell that can develop into nearly all cell types in the body. This includes cells derived from the three primary germ layers: mesoderm, endoderm, and ectoderm, which form early during the differentiation of embryonic stem cells (ESCs). Essentially, pluripotent cells have the ability to give rise to most, if not all, tissues in the body, though they cannot form an entire organism like totipotent cells can.

Multi-Potent Stem Cells

Multipotent stem cells have a more limited ability to differentiate compared to totipotent and pluripotent cells, but they can still give rise to a variety of related cell types. These cells are typically restricted to producing cells from one specific germ layer, such as mesenchymal stem cells (MSCs), which can differentiate into various cell types within the mesoderm, or hematopoietic stem cells (HSCs), which primarily produce blood cells. Adult stem cells also fall into this category. In general, multipotent stem cells are capable of differentiating into a closely related family of cell types, but their potential is more restricted compared to the earlier stages of stem cell differentiation.

Tissue Specific Stem Cell or Adult Stem Cells

Adult stem cells are undifferentiated cells that remain in various tissues throughout the body after embryonic development. They have the ability to multiply and regenerate damaged tissues through cell division. Recent research has shown that adult stem cells might be more versatile than previously thought, with the potential to differentiate into different types of cells from various germ layers. For example, bone marrow stem cells, which come from the mesoderm, can not only produce cells from the mesoderm (like muscle and bone) but also cells from other layers, such as lung, liver, and digestive tract cells (endoderm). Another example is neural

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

stem cells (NSCs), which originate from the ectoderm. These cells have been shown to differentiate into other types of cells, including those from the mesoderm and endoderm. This expanding potential has demonstrated the therapeutic value of adult stem cells, making them increasingly important in cell therapy and regenerative medicine.

Cancer Stem Cells (CSCs)

In the late 1990s, John Dick and his team first identified cancer stem cells (CSCs) in cases of acute myeloid leukemia and other blood cancers. CSCs are a specific type of cancer cell found within tumors or hematologic cancers. What makes them unique is that they share characteristics with normal stem cells, meaning they have the ability to generate all the different types of cells found in a particular cancer. Over time, more and more evidence has supported the cancer stem cell hypothesis, which suggests that, just like normal stem cells help repair and regenerate damaged tissues in the body, CSCs play a similar role in fueling the growth and spread of tumors. Many studies have shown that a tumor's ability to grow and spread depends on a small group of cells with stem-like properties—these are the CSCs.

MSCs

Embryonic connective tissue contains a type of tissue called mesenchyme, from which many different types of connective and blood-forming tissues (hematopoietic tissues) are derived through interactions between the endoderm and ectoderm. However, mesenchymal stem cells (MSCs), despite their broad differentiation potential, do not give rise to blood cells. In 1924, Alexander A. Maximow used detailed histological techniques to identify a specific precursor cell within mesenchyme that could develop into various types of blood cells. MSCs are a unique type of stem cell known for their ability to differentiate into multiple cell types and their capacity for self-renewal. These cells are found in many tissues and organs, including adipose tissue, bone marrow, skin, peripheral blood, the fallopian tubes, cord blood, liver, and lungs, among others.

Today, stem cells are used in a variety of applications, particularly in human therapies like cell transplantation and cell engraftment. In addition to human medicine, stem cell use in veterinary medicine is also gaining attention. The goal of this review is to provide an overview of the different types of stem cells isolated from various animal models, such as horses, pigs, goats, dogs, rabbits, cats, rats, and mice. Given the widespread use and growing interest in MSCs, we will focus particularly on how these cells are being utilized in veterinary medicine.

Application of MSCs in Regenerative Medicine in Animal Models

The wide variety of stem cell sources and their broad potential applications make it challenging to choose the right type of cell for therapy. Animal studies have shown that cell-based therapies, including those using stem cells, can treat a range of diseases. However, there are still concerns about the immune response when using stem cells in therapy. To address these challenges, improving animal models and refining methods for cell transplantation and engraftment are crucial steps toward ensuring the safe and effective use of stem cells in clinical settings.

In this section, we review both current and past studies on the development of animal models that can help advance the use of stem cells in regenerative medicine. Significant progress has been made in stem cell-based therapies, offering new ways to treat diseases that can't be cured with traditional medicine. Stem cells stand at the forefront of regenerative medicine because of their ability to self-renew and differentiate into various cell types, giving them immense therapeutic potential.

A lot of current research focuses on human stem cells, including both embryonic stem cells and adult stem cells, as well as induced pluripotent stem cells (iPSCs), which are reprogrammed from adult cells to behave like embryonic cells. While stem cell therapy has advanced significantly in the last decade, challenges still remain, such as the migration of transplanted cells and poor cell survival after transplantation. To overcome these hurdles, researchers have begun using biocompatible and biodegradable biomaterials in cell therapy. These materials help reduce cell loss and improve the long-term retention of stem cells in the body, which is a critical step in making stem cell treatments more effective and sustainable.

Heart Failure

Heart failure is becoming an increasingly common and serious problem in human populations, with a poor prognosis for many patients. For decades, mesenchymal stem cells (MSCs) have been explored as a potential treatment for heart disease, particularly in regenerative therapies aimed at improving cardiovascular health.

In a study by Dhein et al, bone marrow-derived MSCs (BMSCs) were shown to improve cardiac function in a rabbit model of non-ischemic cardiomyopathy, a type of heart failure. Similarly, in a study by Davies et al, cord blood stem cells were transplanted into a sheep model of heart failure, leading to significant improvements in heart function. The right ventricle showed increased mass, and both systolic and diastolic functions of the heart were enhanced.

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

Another important study by Nagaya et al. found that MSCs could help treat dilated cardiomyopathy (DCM), a condition where the heart becomes enlarged and weakened. The MSCs appeared to promote the growth of new blood vessels (angiogenesis) and reduce fibrosis (scar tissue formation) in the heart, which is critical in preserving heart function.

MSCs are also beneficial in cell transplantation therapies, as they can differentiate into cardiomyocytes (heart muscle cells), vascular endothelial cells (which form blood vessels), and produce factors that reduce cell death (anti-apoptotic) and promote blood vessel growth (angiogenesis).

In 2015, Roura et al. highlighted that umbilical cord blood MSCs (UCBMSCs) could be a promising therapeutic option for conditions involving vascular damage, as these cells have the potential to regenerate blood vessels and support tissue repair.

A study by Ammar et al. compared bone marrow-derived MSCs (BMSCs) and adipose tissue-derived MSCs (ADSCs) in treating heart damage caused by the chemotherapy drug doxorubicin. The results showed that both BMSCs and ADSCs were equally effective in improving heart function. They did so by reducing collagen buildup (which leads to scarring) and promoting the growth of new blood vessels, which helped protect the heart from further damage.

Overall, MSCs show great potential in improving heart health, offering hope for regenerative therapies that could significantly improve the treatment of heart failure and related cardiovascular conditions.

Wound Healing

Chronic wounds are a common and frustrating issue for many patients, causing significant physical and emotional distress. One promising source of stem cells for wound healing is dental tissue-derived MSCs, which are rich in cytokines and growth factors that can promote tissue repair. Previous studies have suggested that stem cells from deciduous teeth (baby teeth) in horses could offer a novel approach for treating chronic wounds and might eventually be used in clinical settings for non-healing wounds.

However, more research is needed to fully understand how these stem cells work, particularly the specific growth factors that play a role in the healing process. Early studies indicate that deciduous teeth-derived stem cells have the potential to support wound healing, as demonstrated in rabbit models of excisional wounds.

In another study, Lin et al. (2013) explored the use of adipose-derived stem cells (ADSCs) in a mouse model. Their findings showed that ADSCs could serve as an effective treatment for full-thickness skin wounds, suggesting they might be a viable option for promoting healing in deep or complex wounds.

These studies highlight the growing interest in using stem cells from various sources to accelerate wound healing, though further research is needed to fully harness their therapeutic potential.

Application of MSCs in Neurodegenerative Disease in Animal Model

As mentioned earlier, stem cells have a wide range of therapeutic applications due to their ability to self-renew and differentiate into various cell types. This gives rise to great hope that stem cell-based therapies can one day treat serious diseases like Alzheimer's, Parkinson's, and other neurodegenerative disorders. In particular, embryonic stem cells (ESCs) are being studied for their ability to differentiate into functional neural cells, which could be used to treat neurological diseases.

A newer category of stem cells, called induced pluripotent stem cells (iPSCs), is also being explored to generate dopamine-producing neurons for Parkinson's disease. In animal studies, such as those using rats, iPSCs have shown potential for developing functional neurons that could help restore lost function in Parkinson's patients. Additionally, neural stem cells (NSCs) and mesenchymal stem cells (MSCs), including those derived from bone marrow, are being tested for their therapeutic potential in treating conditions like Alzheimer's, Parkinson's, and stroke.

For example, bone marrow-derived MSCs (BMSCs) have been shown to reduce brain amyloid deposits and stimulate the activation of microglial cells (which are involved in brain immune responses) in mouse models of Alzheimer's disease. A study by Lee et al. found that BMSCs could increase the number of activated microglia, which helped reduce amyloid-beta (Aβ) deposits—one of the hallmarks of Alzheimer's. Supporting this, Liu et al. showed that transplanting BMSCs into the brains of mice with Alzheimer's led to reduced amyloid-beta buildup, increased levels of brain-derived neurotrophic factor (BDNF, a protein that promotes brain health), and improved social recognition.

Beyond BMSCs, NSCs have also been identified as promising tools for treating neurodegenerative diseases because of their ability to generate appropriate cell types for brain repair. For example, a study by Åkerud et al. demonstrated that NSCs could efficiently

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

produce glial cell line-derived neurotrophic factor (GDNF), a protein that helps protect and repair neurons, suggesting that NSCs could be used in treating diseases like Parkinson's.

In one of the most promising studies, Venkataramana et al. transplanted BMSCs into the brains of seven patients with Parkinson's disease. The results were encouraging, showing potential benefits for patients with this debilitating condition.

These studies underscore the growing potential of stem cells, particularly BMSCs and NSCs, in treating neurological diseases. While more research is needed, these therapies offer hope for future treatments for conditions that currently have few effective options.

CONCLUSIONS

The human body is equipped with a unique group of cells known as mesenchymal stem cells (MSCs), which have the remarkable ability to both self-renew (make copies of themselves) and differentiate into a wide variety of specialized cell types. These include fat cells (adipocytes), bone cells (osteocytes), cartilage cells (chondrocytes), and even nerve cells (neurons). What makes MSCs especially valuable is that, in addition to their ability to regenerate different tissues, they are relatively easy to isolate, can be safely transplanted into injured areas, and have immune-modulating properties, meaning they can help reduce inflammation and promote healing.

Over the years, many studies, both in laboratory settings (in vitro) and in live animal models (in vivo), have shown promising results regarding the potential of MSCs to treat a variety of diseases and injuries. They have been successfully tested in models for conditions like heart failure, wound healing, and even tooth regeneration. These successes suggest that MSCs could one day become a key part of treatments for such conditions in humans.

However, despite these positive findings in animal models, clinical outcomes in humans have not always been as encouraging. While many initial results look promising, translating these successes from animals to humans is a complex process. Challenges like immune rejection, difficulty in controlling the differentiation of stem cells, and ensuring the long-term survival and integration of transplanted cells remain significant obstacles.

One area where MSCs have generated a great deal of interest is in the treatment of neurodegenerative diseases, particularly conditions like Alzheimer's diseas and Parkinson's disease. These are diseases that involve the progressive loss of nerve cells in the brain, leading to symptoms like memory loss, motor dysfunction, and cognitive decline. MSCs hold potential for these conditions because they can support nerve cell regeneration, reduce inflammation, and protect remaining healthy neurons. In both preclinical studies (animal models) and early clinical trials, MSCs have shown promise in promoting neural repair and improving function in conditions like Parkinson's, though more research is needed to refine these treatments.

In summary, MSCs are an exciting and versatile tool in regenerative medicine, with the ability to treat a broad range of diseases. Despite the challenges that remain in translating animal model success into clinical practice, their potential for treating conditions like heart failure, chronic wounds, tooth damage, and neurodegenerative diseases continues to drive research forward. As the science behind MSC therapies improves, these cells could play a key role in revolutionizing the treatment of many debilitating diseases.

REFERENCES

1. *Ghimire S, Weber D, Mavin E, et al. Pathophysiology of gvhd and other hsct-related major complications. **Front Immunol** 2017;8:79. [Crossref] [PubMed]*
2. *Levenberg S, Huang NF, Lavik E, et al. Differentiation of human embryonic stem cells on three-dimensional polymer scaffolds. **Proc Natl Acad Sci U S A** 2003;100:12741-6. [Crossref] [PubMed]*
3. *Takahashi K, Tanabe K, Ohnuki M, et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. **Cell** 2007;131:861-72. [Crossref] [PubMed]*
4. *Lotfinegad P, Shamsasenjan K, Movassaghpour A, et al. Immunomodulatory nature and site specific affinity of mesenchymal stem cells: a hope in cell therapy. **Adv Pharm Bull** 2014;4:5-13. [PubMed]*
5. *Harding J, Roberts RM, Mirochnitchenko O. Large animal models for stem cell therapy. **Stem Cell Res Ther** 2013;4:23. [Crossref] [PubMed]*
6. *Markoski MM. Advances in the use of stem cells in veterinary medicine: from basic research to clinical practice. **Scientifica (Cairo)** 2016;2016:4516920. [Crossref] [PubMed]*
7. *Banas A, Teratani T, Yamamoto Y, et al. Adipose tissue-derived mesenchymal stem cells as a source of human hepatocytes. **Hepatology** 2007;46:219-28. [Crossref] [PubMed]*
8. *Kalra K, Tomar P. Stem Cell: Basics, Classification and Applications. **American Journal of Phytomedicine and Clinical Therapeutics** 2014;27:919-30.*
9. *Mohammadian M, Shamsasenjan K, Lotfi Nezhad P, et al. Mesenchymal stem cells: new aspect in cell-based regenerative therapy. **Adv Pharm Bull** 2013;3:433-7. [PubMed]*

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

10. *Becker AJ, McCulloch EA, Till JE. Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells. **Nature** 1963;197:452-4. [Crossref] [PubMed]*
11. *Song J, Yang D, Ruan J, et al. Production of immunodeficient rabbits by multiplex embryo transfer and multiplex gene targeting. **Sci Rep** 2017;7:12202. [Crossref] [PubMed]*
12. *Friedenstein AJ, Chailakhyan RK, Latsinik NV, et al. Stromal cells responsible for transferring the microenvironment of the hemopoietic tissues: cloning in vitro and retransplantation in vivo. **Transplantation** 1974;17:331-40. [Crossref] [PubMed]*
13. *Fathi E, Farahzadi R. Isolation, culturing, characterization and aging of adipose tissue-derived mesenchymal stem cells: a brief overview. **Brazilian Archives of Biology and Technology** 2016;59.*
14. *Cibelli J, Emborg ME, Prockop DJ, et al. Strategies for improving animal models for regenerative medicine. **Cell Stem Cell** 2013;12:271-4. [Crossref] [PubMed]*
15. *Rippon HJ, Bishop AE. Embryonic stem cells. **Cell Prolif** 2004;37:23-34. [Crossref] [PubMed]*
16. *Kote Amol P, Pawar Sanjay D, Dhonde Satish M, et al. An overview of stem cell. **Pharmacologyonline** 2011;3:1155-70.*
17. *Birbrair A, Frenette PS. Niche heterogeneity in the bone marrow. **Ann N Y Acad Sci** 2016;1370:82-96. [Crossref] [PubMed]*
18. *Takahashi K, Tanabe K, Ohnuki M, et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. **Cell** 2007;131:861-72. [Crossref] [PubMed]*
19. *Goodell MA, Brose K, Paradis G, et al. Isolation and functional properties of murine hematopoietic stem cells that are replicating in vivo. **J Exp Med** 1996;183:1797-806. [Crossref] [PubMed]*
20. *Levenberg S, Huang NF, Lavik E, et al. Differentiation of human embryonic stem cells on three-dimensional polymer scaffolds. **Proc Natl Acad Sci U S A** 2003;100:12741-6. [Crossref] [PubMed]*
21. *Waghmare, Siddhesh G., and Ameetul Noor Zeba Khannam. "UNDERSTANDING STEM CELLS: PRINCIPLES AND ADVANCES IN REGENERATIVE THERAPY."*