

Brief essay on neuroregenerative medicine: approaching a new era through stem cell therapy techniques

Abstract

Neurodegenerative diseases, such as Alzheimer's, Parkinson's, and spinal cord injuries amongst others pose significant challenges to modern Medicine. Traditional treatments often focus on symptom management rather than targeting the root causes of these conditions. However, the advent of Neuroregenerative Medicine represents a cutting-edge field that aims at restoring the structure and function of the nervous system, particularly in cases of injury or degenerative diseases. Stem Cell therapy techniques have excitingly emerged as a promising avenue in this domain, offering the potential to repair damaged neural tissue, promote its regeneration, and restore lost function. This brief essay explores the principles behind Neuroregenerative Medicine and highlights the applications, challenges, and prospects of Stem Cell therapy in treating neurodegenerative disorders.

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Introduction

The field of Neuroregenerative Medicine has garnered significant attention in recent years due to its potential to address the unmet medical needs of patients suffering from neurological disorders and injuries.^{1,2} These conditions, ranging from spinal cord injuries to neurodegenerative diseases, present complex challenges for conventional treatments.³ However, Stem Cell therapy techniques offer a promising approach to restore function and enhance the life quality of the affected individuals.⁴ This is a comprehensive overview of Neuroregenerative Medicine, with a focus on the role of Stem Cell therapies in revolutionizing the field.

Principles of neuroregenerative medicine

Neuroregenerative Medicine aims at restoring lost or damaged neural tissue through the activation of endogenous repair mechanisms or the introduction of exogenous factors that promote tissue regeneration.^{3,5,6} Central to this field are *stem cells*, which possess the remarkable ability to self-renew and differentiate into various specialized cell types.⁷ Stem cells serve as the building blocks for tissue regeneration, providing the means to repair and replace damaged neural cells.⁸

There are different types of stem cells utilized in neuroregenerative Medicine, each with its unique properties and potential applications.⁹ *Embryonic stem cells* (ESCs) (Figure 1), derived from early-stage embryos, are pluripotent cells capable of differentiating into any cell type in the body. *Induced pluripotent stem cells* (iPSCs) (Figure 2), reprogrammed from adult cells, share similar properties to ESCs and offer a patient-specific approach to therapy. *Adult stem cells* such as *neural stem cells* and *mesenchymal stem cells* reside in various tissues throughout the body and have a more restricted differentiation potential. Additionally, *cord blood stem cells*, harvested from umbilical cord blood, have shown potential in treating certain neurological conditions (Figure 3).¹⁰

Stem cell therapy techniques

Stem cell therapy techniques encompass various approaches for utilizing stem cells to regenerate neural tissue.¹¹ *Embryonic stem cell therapy* involves the use of ESCs to replace damaged or lost neurons.¹² This approach holds immense potential but is accompanied by ethical considerations and challenges associated with immune rejection. Induced pluripotent stem cells offer a patient specific alternative by reprogramming adult cells into pluripotent stem cells, eliminating ethical concerns, and mitigating immune rejection risks.⁹

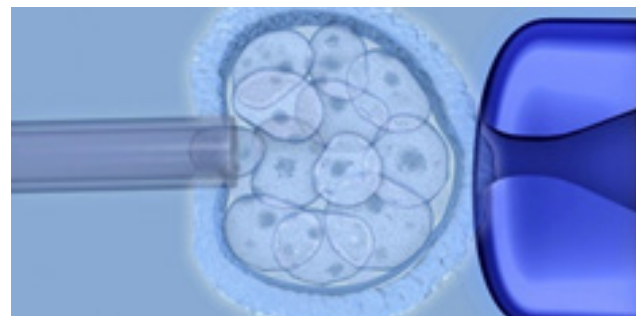


Figure 1 Embryonic stem cells.

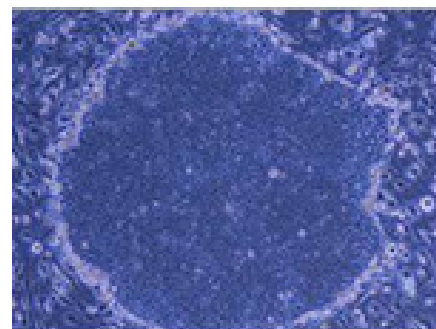


Figure 2 Induced pluripotent stem cells.

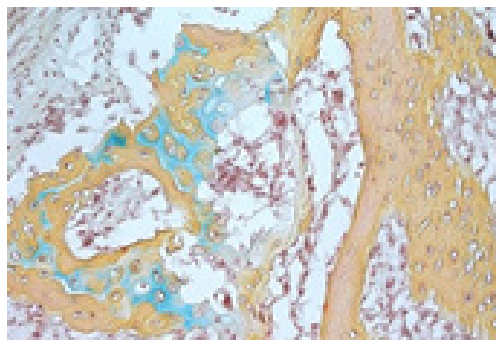


Figure 3 Adult stem cells.

Adult stem cells have also shown promise in neuroregenerative Medicine. *Neural stem cells* (NSCs) have the capacity to differentiate into various neural cell types, making them a valuable resource for repairing damaged neural circuits.¹³

Mesenchymal stem cells (MSCs), derived from sources such as bone marrow or adipose tissue, possess immunomodulatory properties and can aid in tissue repair by promoting neuroprotection and reducing inflammation.

Cord blood stem cells, obtained from the umbilical cord and placenta, represent another source of stem cells used in neuroregenerative therapies. These cells can be isolated and stored for future use, providing a readily available source of cells with the potential to differentiate into neural lineages.¹⁴

Applications of stem cell therapy in neuroregenerative medicine

Stem Cell therapy holds immense potential in the treatment of various neurodegenerative diseases. In Alzheimer’s disease,¹⁴ stem cells can potentially replace lost neurons and enhance cognitive function. Parkinson’s disease, characterized by the loss of dopamine-producing neurons, may benefit from stem cell transplantation to restore the damaged nigrostriatal pathway.^{11,15} Spinal cord injuries, often resulting in permanent motor and sensory deficit, present an opportunity for neural regeneration using stem cell-based approaches. Similarly, stroke and multiple sclerosis, with their debilitating consequences, can be targeted using stem cell therapy to promote functional recovery and mitigate disease progression (Figure 4).

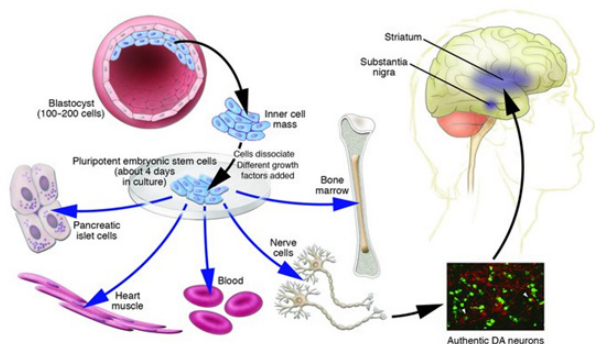


Figure 4 Pluripotent embryonic stem cells are obtained from the inner cell mass of the blastocyst stage of development.

Challenges and limitations

Despite the immense potential of Stem Cell therapy in neuroregenerative medicine, several challenges and limitations need to be addressed for its widespread implementation. Ethical considerations surrounding the use of embryonic stem cells remain a contentious issue, necessitating ongoing ethical discourse and careful regulation. The potential for immune rejection in stem cell transplantation requires strategies to mitigate graft rejection and improve long-term engraftment.¹⁶ Additionally, the tumorigenic potential of pluripotent stem cells and the need for standardized procedures pose significant hurdles to overcome. Regulatory frameworks must be established to ensure patient safety and therapeutic efficacy.

Advances in stem cell research

Recent advancements in stem cell research have propelled the field of Neuroregenerative Medicine forward.^{17,18} Genetic engineering techniques enable the modification of stem cells to enhance their survival, integration, and differentiation capacities. 3D bioprinting (Figure 5), combined with stem cells, allows the fabrication of complex neural tissue structures, facilitating the development of functional neural grafts. Biomaterials and scaffolds provide physical and biochemical support to transplanted stem cells, creating a conducive environment for their integration and maturation.¹⁹

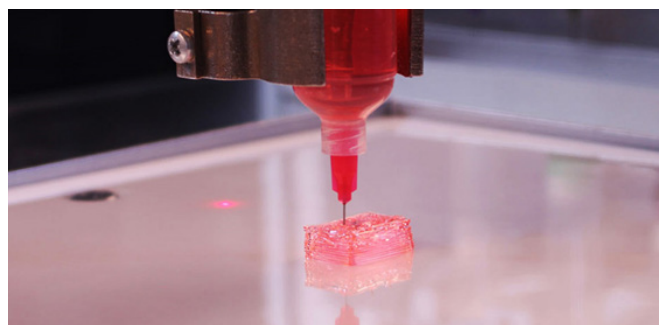


Figure 5 Stem Cells 3D Bioprinting.

Clinical trials and success stories

Clinical trials investigating the safety and efficacy of Stem Cell therapy in Neuroregenerative Medicine have demonstrated great results. Notable trials have focused on Alzheimer’s disease, Parkinson’s disease, spinal cord injuries, stroke, and multiple sclerosis.^{20,21} These trials have shown improvements in motor function, cognitive abilities, and quality of life in some patients.²² Additionally, patient testimonials and case studies highlight the transformative potential of stem cell therapy in restoring lost function and improving overall well-being.

Future prospects and emerging technologies

The future of Neuroregenerative Medicine holds exciting prospects and opportunities. Precision medicine approaches, tailored to an individual’s genetic profile and disease characteristics, could enhance treatment outcomes.^{23,24} Combination therapies, combining stem cell transplantation with other modalities such as gene therapy or pharmacological interventions, may yield synergistic effects.^{25,26} Artificial intelligence can aid in the identification of optimal stem cell sources, differentiation protocols, and personalized treatment strategies. Gene editing techniques, such as CRISPR-Cas9 (Figure 6), offer precise genome modifications and may contribute to enhanced stem cell therapies.^{27,28} Novel delivery methods, including targeted nanoparticles or exosomes, may improve the delivery and engraftment of stem cells within the central nervous system.²⁹

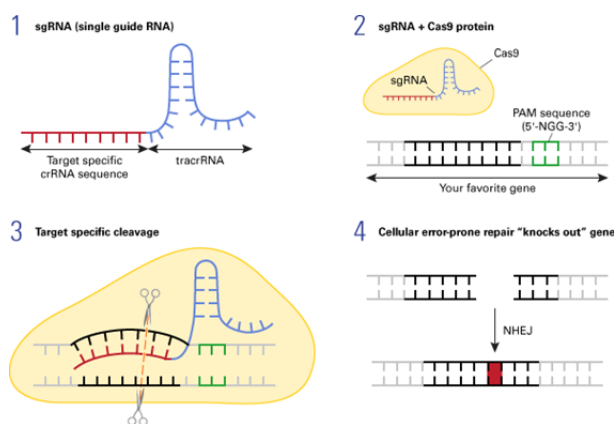


Figure 6 CRISPR/Cas9 system.

Ethical considerations and public perception

The ethical considerations surrounding Stem Cell therapy, particularly the use of embryonic stem cells, require ongoing debate and regulation.³⁰ Public awareness and education initiatives are vital to address misconceptions and foster informed discussions. Balancing scientific progress with ethical concerns is crucial to ensure responsible and ethically sound research practices. Regulatory bodies must develop comprehensive guidelines to govern the use of stem cell therapy and maintain patient safety.

Conclusion

Neuroregenerative Medicine, with its focus on harnessing the potential of stem cells, offers hope for the treatment of neurodegenerative diseases. Stem Cell therapy techniques hold unique potential in restoring lost neural function and repairing damaged tissue. Although challenges and limitations persist, advancements in stem cell research, clinical trials, and emerging technologies provide a strong foundation for the future of Neuroregenerative Medicine. With continued research, innovation, and responsible practices, Stem Cell therapy has the potential to revolutionize the medical field and improve the lives of millions affected by neurodegenerative disorders.

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None.

Conflicts of interest

The authors declare no conflicts of interest.

References

- Martino G, Pluchino S. The therapeutic potential of neural stem cells. *Nat Rev Neurosci.* 2006;7(5):395–406.
- Azari H, Rahman M, Shariffar S, et al. The combined application of stem cells and tissue engineering: a novel approach for the treatment of spinal cord injuries. *Int J Mol Sci.* 2018;19(4):935.
- Goldman SA. Stem and progenitor cell-based therapy of the central nervous system: hopes, hype, and wishful thinking. *Cell Stem Cell.* 2016;18(2):174–188.
- Bjugstad KB, Freed CR. Stem cell-based therapy for Parkinson's disease: promises and challenges. *Prog Brain Res.* 2017;230:141–157.
- Lindvall O, Kokaia Z. Stem cells in human neurodegenerative disorders—time for clinical translation? *J Clin Invest.* 2010;120(1):29–40.
- Nagai M, Re DB, Nagata T, et al. Astrocytes expressing ALS-linked mutated SOD1 release factors selectively toxic to motor neurons. *Nat Neurosci.* 2007;10(5):615–622.
- Park D, Xiang AP, Mao FF, et al. Nestin is required for the proper self-renewal of neural stem cells. *Stem Cells.* 2010;28(12):2162–2171.
- Kokaia Z, Lindvall O. Neurogenesis after ischaemic brain insults. *Curr Opin Neurobiol.* 2003;13(1):127–132.
- Vescovi AL, Parati EA, Gritti A, et al. Isolation and cloning of multipotential stem cells from the embryonic human CNS and establishment of transplantable human neural stem cell lines by epigenetic stimulation. *Exp Neurol.* 1999;156(1):71–83.
- Yan Y, Ma T, Gong K, et al. Pluripotent potential of adult neural stem cells. *Cell Transplant.* 2013;22(5):807–816.
- Barker RA, Götz M, Parmar M. New approaches for brain repair—from rescue to reprogramming. *Nature.* 2018;557(7705):329–334.
- Weiss S, Dunne C, Hewson J, et al. Multipotent CNS stem cells are present in the adult mammalian spinal cord and ventricular neuroaxis. *J Neurosci.* 1996;16(23):7599–7609.
- Tetzlaff W, Okon EB, Karimi–Abdolrezaee S, et al. A systematic review of cellular transplantation therapies for spinal cord injury. *J Neurotrauma.* 2011;28(8):1611–1682.
- Cui Y, Ma S, Zhang C, et al. Human umbilical cord mesenchymal stem cells transplantation improves cognitive function in Alzheimer's disease mice by decreasing oxidative stress and promoting hippocampal neurogenesis. *Behav Brain Res.* 2017;320:291–301.
- Wijeyekoon RS, Barker RA. Cell replacement therapy for Parkinson's disease. *Biochim Biophys Acta.* 2009;1792(7):688–702.
- Kokaia Z, Martino G, Schwartz M, et al. Cross-talk between neural stem cells and immune cells: the key to better brain repair? *Nat Neurosci.* 2012;15(8):1078–1087.
- Yasuhara T, Matsukawa N, Hara K, et al. Transplantation of human neural stem cells exerts neuroprotection in a rat model of Parkinson's disease. *J Neurosci.* 2006;26(48):12497–12511.
- Hasegawa T, McInnes J, Ivanovski S. Regenerative periodontal therapy: recent advances, current status, and future directions. *Periodontol 2000.* 2019;79(1):238–252.
- Kim HJ, Lee JH, Kim SH. Therapeutic effects of stem cells in animal models of neurodegenerative disease: a meta-analysis. *Neurosci Biobehav Rev.* 2017;73:396–405.
- Lu P, Jones LL, Tuszynski MH. Axon regeneration through scars and into sites of chronic spinal cord injury. *Exp Neurol.* 2007;203(1):8.
- Quan DN, Hassell TP, Popovic EA, et al. Human embryonic stem cell-derived mesenchymal progenitors repair spinal cord injury in rodents. *Stem Cell Res Ther.* 2015;6:110.
- Teng YD, Lavik EB, Qu X, et al. Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells. *Proc Natl Acad Sci U S A.* 2002;99(5):3024–3029.
- Lindvall O, Kokaia Z, Martínez–Serrano A. Stem cell therapy for human neurodegenerative disorders—how to make it work. *Nat Med.* 2004;10(7 Suppl):S42–S50.
- Bonfanti L. From hydra regeneration to human brain structural plasticity: a long trip through narrowing roads. *Sci Transl Med.* 2011;3(74):74ps10.
- Martino G, Schwartz M. CNS immunology and neuroimmunology: from discovery to dual therapy for neurological disease. *Nat Rev Neurol.* 2019;15(9):483–495.
- Lu P, Tuszynski MH. Growth factors and combinatorial therapies for CNS regeneration. *Exp Neurol.* 2008;209(2):313–320.

27. Pittenger MF, Mackay AM, Beck SC, et al. Multilineage potential of adult human mesenchymal stem cells. *Science*. 1999;284(5411):143–147.
28. Nicaise AM, Banda E, Guzzo RM, et al. iPS-derived neural progenitor cells from PPMS patients reveal defect in myelin injury response. *Exp Neurol*. 2019;311:271–284.
29. Sofroniew MV. Molecular dissection of reactive astrogliosis and glial scar formation. *Trends Neurosci*. 2009;32(12):638–647.
30. Chopp M, Zhang XH, Li Y, et al. Spinal cord injury in rat: treatment with bone marrow stromal cell transplantation. *Neuroreport*. 2000;11(13):3001–3005.