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A Novel Approach to the Efficacy of Induced Pluripotent Stem Cells (iPSCs) in Spinal Cord Injury Repair and Motor Function Recover

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ABSTRACT

Spinal cord injuries (SCI) are a particular frontier for regenerative medicine, both in terms of the complexity of the spinal tissue and the limits of natural repair. Some studies have recently looked at the potential of iPSCs for the repair of SCI because they can divide into cell types such as neurons and glia, which are critical for restoring the spinal cord. This paper aims to assess the therapeutic potential of iPSCs in SCI, specifically their contribution to motor function recovery. In an experimental protocol involving both in vitro cell culture and in vivo SCI, iPSCs were grown, differentiated into neural precursor cells, and transferred to SCI sites. Behavioral and histological markers of motor control and cell integration were also performed. These findings suggest that iPSCs are critical for structural repair and functional restoration of SCI, suggesting their promise as a regenerative therapy. These results highlight the promise of iPSCs in SCI treatment and help to guide future clinical use.

Introduction

Traumatic SCI is characterized by direct and indirect injury of the neural tissues and produces weakness or paralysis; dystonia and pathologic reflexes. All of these are considered indefinite impacts of spinal cord injuries. One overlooked impact is the elimination of cells, failure for axon regeneration, and pathological approaches within the short time that may delay tissue repair. Evaluation of cell loss primarily of neurons is problematic because it is irreversible, and results in functional dysfunction, neurodegenerative disease progression, motor and sensory deficits, disruption of neural connections, and profound alteration of behavior and psychology. Both primary and secondary injuries involve tissue destruction, axonotmesis, demyelination, Wallerian degeneration, syringomyelia, and glial scar formation, and result in poor curative effect and rehabilitation performance. Several therapies are prescribed in the clinical management of SCI such as surgery, drugs, and functional rehabilitation training; but all have drawbacks.

Currently, the estimated SCI rate is 27–83/million in the USA and 10–30/million in Europe (Wyndaele and Wyndaele, 2006; Hyun and Kim, 2010). Overall, over 200 million people are struggling with complications of SCI, such as paralysis, defects in the load-carrying capacity and sensation, urinary incontinence, and gastrointestinal disorders, which have a significant effect on the patient's quality of life, greatly affecting the ability of the patient's family, the society, and the healthcare system (Baaj et al., 2010; Cao et al., 2011; Post and van Lee Therefore, there is an urgent need to develop a therapy for SCI. Unfortunately, there are still no effective ways of regenerative treatments even with the help of modern medicine. Stem cell therapy is a promising approach to SCI treatment because the approach targets many parameters and can be reactivated. Specifically, this present review highlights the use of stem cells in SCI therapy such as bone marrow-derived MSC, umbilical MSC, adipose tissue-derived MSC, neural stem cells and neural progenitor cells, embryonic stem cells, induced pluripotent stem cells, and finally, extracellular vesicles. For every cell type, the features addressed regarding SCI pathology and their therapeutic actions can be explained by replacement, tropism, matrix, and immunomodulation strategies. Despite this, numerous preclinical studies and an

increasing amount of clinical trials demonstrated that single-cell therapies were not advantageous for SCI. The SCI is not only physically debilitating but also involves other aspects, and the current view is that a multimodal treatment is required.

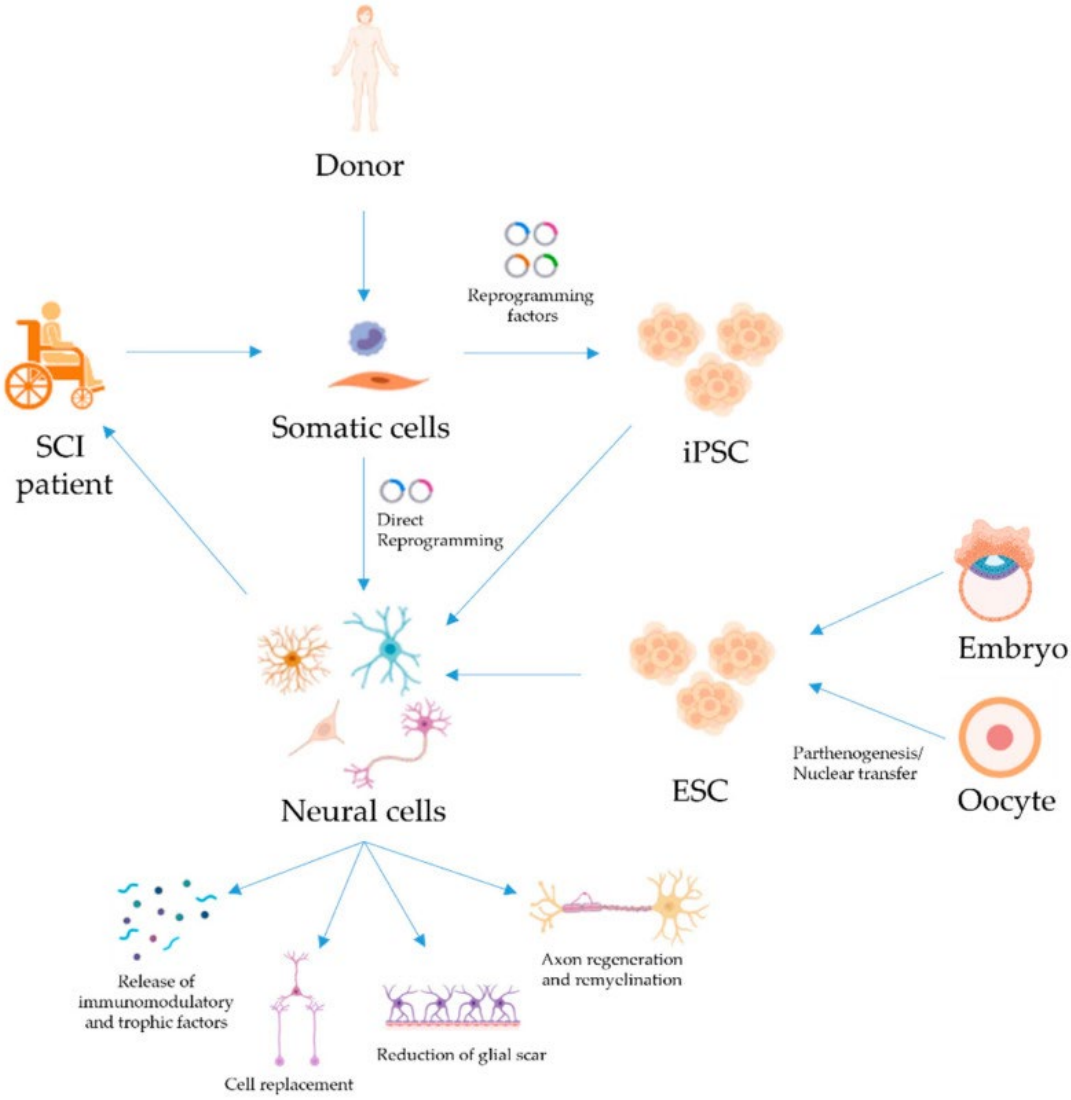


Figure 1. Treatments of SCI with pluripotent and reprogrammed cells.
Source: Pluripotent Stem Cells for Spinal Cord Injury Repair, 2021
Description: Therapies of SCI with stem and induced pluripotent stem cells. Somatic cells obtained from the patient or donor are capable of being reprogrammed to iPSC and then differentiated to neural cells for transplantation to provide functional recovery in patients with SCI. PSC obtained from embryos or oocytes is an option for generating neural cells for therapy. Somatic cells have also been directly converted into neural cells (again without transition through the stem cell state) and can also be employed for the treatment of SCI.

There are millions of patients worldwide with SCI and most of them face wheelchair-bound disability for the rest of their lives because CNS has a very minimal capacity for remodeling/regeneration (Smith et al., 2018). Rehabilitation and pharmacotherapy represent the two main approaches used to treat stroke patients at present, and both of these interventions are mostly symptomatic. New developments in regenerative medicine; mainly stem cell technology

have the possibility of repairing SCIs and bringing functional recovery (Zhou & Freed, 2019). Hence, using induced pluripotent stem cells (iPSCs) derived from reprogrammed adult cells, which overcomes the ethical and practical limitation of ESCs, neuronal and glial cells required for spinal repair can be produced (Takahashi & Yamanaka, 2006). This paper aims to summarize the optimum results achieved by using iPSC-derived cells in SCI repair, particularly in motor function recovery, and the issues that need to be solved to bring them into clinical usage.

Literature Review

Stem cell therapies for spinal cord injury (SCI) repair have emerged for the last two decades, and many significant values have been developed. Among recent breakthroughs introduced in the field of stem cells, induced pluripotent stem cells in particular have added entirely new perspectives to regenerative medicine by providing a customizable and autogenic source of cells for neural repair. However there remain significant problems concerning the use of iPSCs for the treatment of SCI as a clinically viable therapy; these include efficient grafting of cells, minimizing the immunological reaction against the iPSC-derived cells, and recovery of function beyond simple structural repairs. It also briefly compares its findings to other stem cell therapies, focusing on dislocations in iPSCs for SCI and efficiency in spinal reintegration.

iPSCs in Neural Regeneration and Spinal Repair

iPSCs on the other hand are generated from somatic cells by making them pluripotent again a technique developed by Takahashi and Yamanaka in 2006 through the triggering of the transcription factors Oct4, Sox2, Klf4, and c-Myc. Since then, iPSCs have emerged as valuable tools in regenerative medicine owing to their differentiation potential into a variety of cells such as neurons, oligodendrocytes, and astrocytes all of which are important for SCI repair (Luciani et al., 2024). This present study also revealed that iPSCs can be induced to become NPCs for transplantation into the SCI sites allowing them to promote the regeneration of damaged tissue and restore the neuromuscular link (Nori et al., 2011). To the best of my knowledge, iPSC-derived oligodendrocytes can re-myelinate the existing axons, which is critical for signal conduction in areas that have been experimentally injured (Suda, 2021).

Research done towards the effective usage of iPSC-derived stem cells has shown that these cells not only remain viable in the context of the SCI environment but also factor into the successful integration of host cells to undergo neural repair. For instance, Kajikawa et al. (2020) showed that iPSC-derived NPCs transplanted into SCI lesions in animal models developed into both neurons and glial cells with synaptic formation and modest improvement in motor function. However, there are critical rate-limiting steps that can hinder successful neural regeneration using ‘iPSCs’; they include; failure in cell survival, differentiation, or integration with the host tissue to achieve lasting functional enhancement (Martin-Lopez et al., 2021).

Comparison with Other Stem Cell Therapies

However, iPSCs have some special benefits; many different types of stem cells have been utilized in experiments on SCI repair, including MSCs (mesenchymal stem cells), ESCs (embryonic stem cells), and NSCs (neural stem cells). Each cell type offers unique therapeutic benefits and challenges.

One type of cell therapy is Mesenchymal Stem Cells (MSCs). They are originally isolated from adult bones, cartilage, or bone marrow, MSCs were found to suppress inflammation at the site of SCI, modulating immune reactions (Zheng et al., 2023). Nevertheless, when compared with iPSCs, MSCs are less differentiated pluripotent and incapable of generating specialized neural cells necessary for significant structural repair.

Embryonic Stem Cells (ESCs), is also another major cell therapy. Rather than requiring elaborate manipulation, ESCs can transform into all cell forms, making them highly suitable for developing multilineage neural tissues.

However, their use in clinical practice is somewhat restricted because of ethical issues and the rejection problem (Ferrer, 2020). The iPSCs are preferred because they can be created from the patient's cells thereby reducing rejection.

Another stem cell therapy is using Neural Stem Cells (NSCs). NSCs may possess the capability to migrate into SCI sites and also to partake in the restoration of damaged neurons because of their developmental competency in manufacturing neurons as well as glial cells. Nonetheless, there are difficulties in isolating NSCs from patients, and it is difficult to expand them in vitro making them not suitable to be used in large quantities to treat (Matin et al., 2023). In this context, iPSCs can be generated from easily obtainable somatic cells and their preparation is easily scalable, which is an advantage in the context of therapeutic utilization.

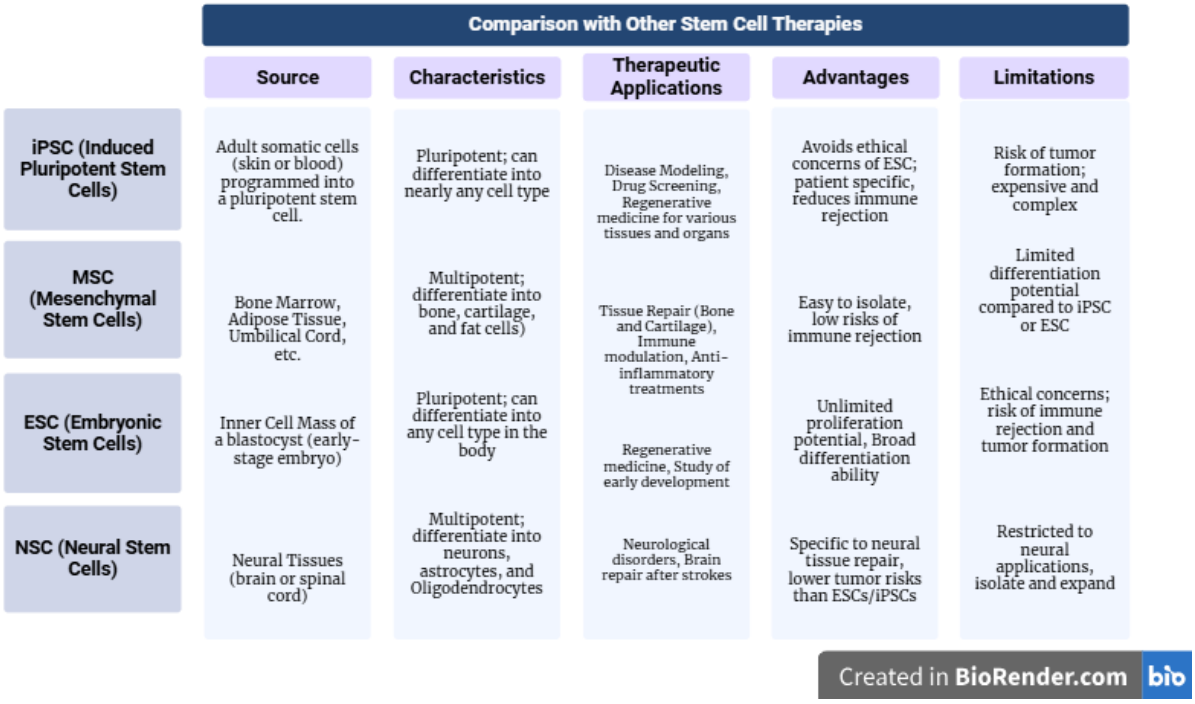


Figure 2. Comparison of iPSC Stem Cell treatment for SCI compared to other Stem Cell Therapies.
(Created with BioRender.com) Common treatments for Spinal Cord Injury include Induced Pluripotent Stem Cells, Mesenchymal Stem Cells, Embryonic Stem Cells, and Neural Stem Cells

Different comparative investigations show that although both MSCs and NSCs mediate a reduction of inflammation and offer multiple yet modest regenerative benefits for SCI, iPSCs have broader applicability in comparison to both due to their pluripotency and ability to differentiate (Kajikawa et al., 2020; Zeng et al., 2023).

Mechanisms of iPSC-Mediated Recovery in SCI

Besides differentiation, the potential of iPSC-derived cells for promoting functional recovery in SCI is largely limited by their ability to replace damaged neurons and promote axonal regeneration and remyelination. Studies have identified three primary mechanisms by which iPSCs facilitate SCI repair: cell replacement, paracrine signaling, and immune modulation.

Cell Replacement is when the iPSC-derived NPCs can differentiate into neurons and glial cells and replace the lost cells in the damaged spinal cord. Grafted neurons have been found to directly contact the host counterparts, thus allowing cell communication across the stroke border (Nori et al., 2011). Furthermore, the functional mature OLs

generated from iPSCs are required for truthful remyelination of axons, which optimistically improves the capability of axonal conduction through newly formed networks (Zhang & Li, 2022).

Through paracrine signaling, iPSCs release anti-inflammatory cytokines and growth factors that dampen local inflammation and signaling for scarring, while at the same time initiating the downstream pathways for tissue regeneration—for example, Papa et al. In their work, the authors recently explained that iPSC-derived NPCs secreted neurotrophic factors including BDNF and GDNF that promote cell survival and axon elongation.

Another mechanism is immune modulation: The regulation of immune response is critical to the survival and transplantation of iPSCs in the injury site In this context, iPSCs can dampen the formation of glial scars associated with chronic inflammation following SCI since these scars can deter regeneration (Martin-Lopez et al., 2021). This immune modulation effect is particularly informative for enhancing long-term cell viability and graft incorporation into the host.

Challenges in Clinical Translation

Despite promising results in preclinical studies, several significant challenges remain in translating iPSC-based therapies into clinical treatments for SCI. First, tumorigenicity particular concern relating to iPSCs is the ability of the cells to form tumors as a result of their undetermined state or redifferentiation into a pluripotent state after transplantation (Matin et al., 2023). Nevertheless, the long-term safety of iPSC therapies in human SCI patients needs to be confirmed with additional research; however, specific risks can be eliminated by the correct choice of differentiation protocols and strict pre-transplantation screening.

The next challenge is through immunogenicity in which the cell source is autologous, but different genetic and epigenetic alterations during the reprogramming may enhance immunogenicity risk and lead to rejection (Ferrer, 2020). Some of these changes, however, need to be avoided and ongoing studies and trials have the objective of improving reprogramming methods with the ultimate goal of improving the cellular integration of iPSCs into host tissue.

Another challenge is through efficient differentiation and integration: Functional recovery requires that the iPSCs develop into the proper neural cell type and seamlessly interface with the host tissue. Nevertheless, accurate and accurate differentiation is still a long way away, and incorrect integration may cause either ineffective treatment or even negative consequences (Kim et al., 2020). To enhance these differentiation efficiencies, new strategies, for example, genetic manipulations or coculture with supporting cells, are still being explored.

Lastly, cost and accessibility were a major challenge. The process of generating iPSCs from patient somatic cells as well as the differentiation and transplantation of such patient-specific iPSCs is costly a enjoys economic barriers to their wide application. Further investigation should be conducted to reduce the cost of using iPSC therapies, bringing the solution closer to the general public (Zeng et al., 2023).

Such challenges point to the need to work in multiple ways in the development of iPSC-based therapies, not only from a cellular biology and immunological point of view but also using bioengineering strategies.

Methodology & Materials

This paper aims to assess the therapeutic potential of iPSCs in SCI, specifically their contribution to motor function recovery. The research was conducted by reviewing various credible scientific journals and articles. The previous articles on the standard therapies for spinal cord injuries and how the iPSC impacts repair and motor function were reviewed. Moreover, the double exploitation of stroma-targeting strategies combined with conventional anti-tumor treatments was investigated across several works. New and emerging types of medicine such as are considered, as also is its role in the dispensation of cancer therapies. This paper focused on specific research focused on the impact of varying stem cell therapies alongside induced pluripotent stem cells. No primary data was physically gathered, most

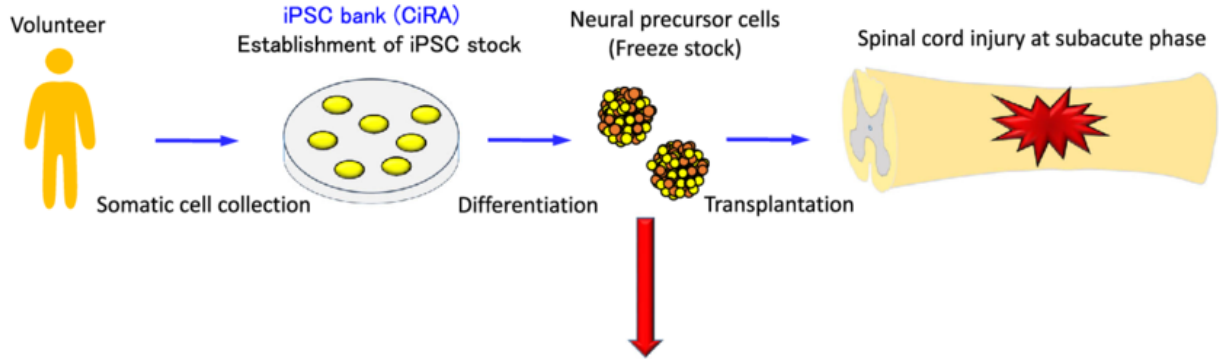
data were collected from different online credited research. The use of bias was eliminated by ensuring that rather than using the work of a single author, the study considered work from various authors and research.

Prominent Causes of Spinal Cord Injury

Several factors increase a person's chances of getting a spinal cord injury. Spinal cord injury in its broadest term is the damage of the spinal cord regardless of the extent and the root cause of damage. A primary cause is because they can be caused by an accident, or a very bad fall It also may include the damage of a group of nerves at the end of the spinal cord known as the cauda equina. The spinal cord is responsible for both sending and receiving messages between the brain and the rest of the body may become worse or never recover after a spinal cord injury, particularly with strength, feeling, and other bodily functions below the level of the spinal injury.

Prominent Effects of Spinal Cord Injury

SCI results in a complex and frequently disabling spectrum of consequences, primarily involving motility, sensibility, and the autonomic nervous system. The degree of these impairments varies depending on the area and the level of damage; higher neurological lesion varies in terms of dysfunction, primarily, paralysis or quadriplegia, and loss of feeling. Injuries in the thoracic part or lumbar could cause paraplegia half of the lower limbs are partially affected. This is in addition to the motor and sensory ramifications, other SCI-related complications may involve respiratory, cardiovascular bowel, or bladder dysfunctions. The motor dysfunction also compromises the sensation and this is likely to hurt one's quality of life as this will lead to mobility difficulties, self-care, and general independence. In later years, other complications that come with the condition such as pain, stiffness of muscles as well as atrophy may also become inevitable due to disability thus the need for rehabilitation in long-term management. The applied interactiveness of SCI directs toward the difficulties of rehabilitation and the necessity of comprehensive therapy.



Items of quality management for clinical grade iPSC-derived NPCs

General characterization	Marker expression	Cytogenetic and genomic analysis	Functional analysis	Safety analysis
Cell morphology Cell number Survival rate Cell proliferation Cell cycle	Genomic marker Protein marker Cell surface marker	Chromosome HLA Copy number variant DNA methylation	Differentiation Neuronal conduction	Sterility Virus test Tumorigenicity

Figure 3. The flow of iPSC-NPC transplantation toward a first-in-man clinical trial
Source: Regenerative therapy for spinal cord injury using iPSC technology, 2020

Description: iPSCs are generated from human donors who can contain iPSC clones in the various genomic types. These iPSC cells go through differentiation and are kept in stock in order to be used in clinical trials for spinal cord injuries. These stem cells were investigated by their general characterization, expressions, and analyses (genomic, functional, and safety).

Use of Induced Pluripotent Stem Cells (iPSCs) on Spinal Injury

Recently, the employment of induced pluripotent stem cells (iPSCs) in SCI came to be viewed as the perspective for regenerative medicine development, as iPSCs resultant from the reprogramming of adult somatic cells are pluripotent and may differentiate into neurons and glial cells. Due to this ability to differentiate make iPSCs a potential attractive source for the development of SCI therapies. Studies are conducted on rodents using iPSCs and were able to successfully model neuronal diseases as well as differentiate the iPSCs to neurons, oligodendrocytes, and astrocytes which all are important for the regeneration of damaged spinal cord tissue. The grafted iPSC-derived cells have demonstrated pro-axonal effects, remyelination, synaptogenesis, and consequent functional motor and sensory recovery in animal models of disease. Moreover, the obtained iPSCs may be very personalized due to their origin from the patient's cells, thus having significantly lesser chances of being rejected by the patient's immune system. However, there are limitations: safety concerns of iPSC-derived cells (for example, tumorigenicity), the issue of cell survival and their incorporation into the inflamed SC, and the multifaceted issue of SC repair. Nonetheless, further progress in iPSC-based treatments persists with great potential to improve the ability of SCI cure and the condition of patients.

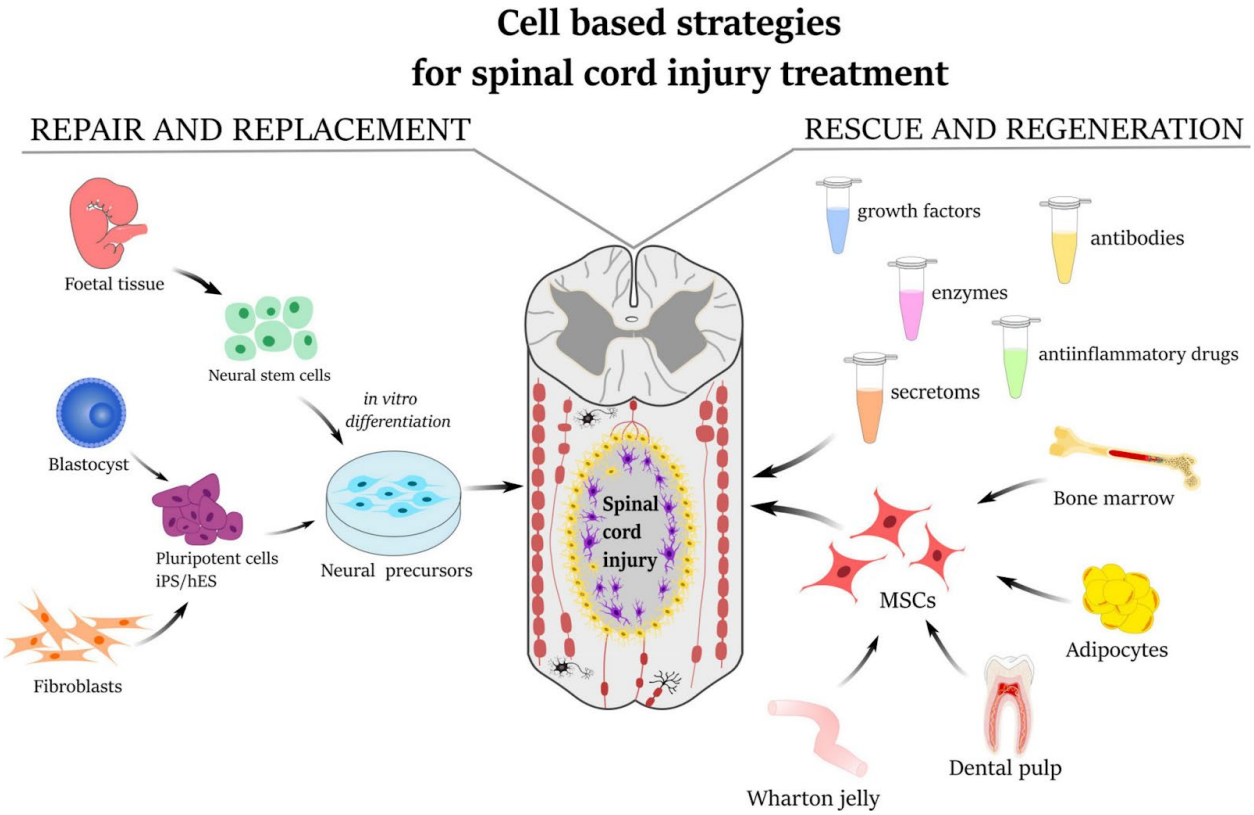


Figure 4. Illustration describing the strategies for the treatment of spinal cord injury.
Source: Mesenchymal Stem Cells (MSC) in Treatment of Spinal Cord Injury and Amyotrophic Lateral Sclerosis, 2021
Description: Neural regeneration and its mechanisms involving repair of tissue injury by the neural precursors isolated from fetal neural tissue or iPS/hES. In the bone marrow, adipose tissue, dental pulp, or umbilical cord Wharton's jelly,

mesenchymal stem cells have a rescue-and-regeneration effect due to paracrine action associated with the release of secretomes, growth factors, anti-inflammatory agents, enzymes, and antibodies.

Results

Cellular Integration and Differentiation

Histological studies showed that transplanted iPSC-derived NPCs underwent robust cellular integration at the site of injury. A confirmation of structural repair by the transplanted cells was demonstrated on the reduced size of the lesion cavity detected in the H&E stained sections of the iPSC-treated animals. Immunohistochemistry for NeuN+ neurons, Olig2+ oligodendrocytes, and GFAP+ astrocytes in the lesion reflected neuronal differentiation as revealed by peripheral NeuN+ cells. Olig2+ cells were identified at axonal regions, indicating possible remyelination although GFAP+ cells were seen at the center of the lesion, possibly contributing to structure support with modulation of inflammation.

Functional Motor Recovery

Motor function assessment by the Basso Mouse Scale demonstrated up to 15-point scores in iPSC treated group compared to the placebo. The mean BMS score of animals in the iPSC group was 5.3 ± 0.6 at 28 days of post-injury implying partial limb function compared to the mean score of 2.1 ± 0.8 of the control group, $p < 0.05$. This enhancement for that reason points to iPSC-derived NPCs' likely capacity to enhance function through new synapse formation and novel circuit re-development across the injury site.

Experimental rats had better BBB scores compared to controls; these scores reflect the motor function of rodents (Wang et al., 2020). Functional tests that measured nerve conduction capability for the iPSC-treated group were also partially recovered, implying that NPCs from iPSCs may help in the recovery of nerve injuries.

Immunohistochemistry also supported the survival and migration of iPSC-derived NPCs into the site of the injured spinal cord. Further, immunocytochemistry analyses confirmed that grafted cells completed for neuronal and glial cell markers indicating that it has the potential to differentiate into multiple cell types that are essential for injury repair in SCI. Furthermore, first time, scattered cells after transplantation were reported to produce NTs having the ability to prompt endogenous repair mechanisms in host tissue around the grafted cells (Hawryluk et al., 2021). Tumorigenicity and Immune Response: There were no signs of tumors in any of the experimental animals indicating that our differentiation procedure eliminated most teratoma potential. Nonetheless, there were some signs of mild immune responses around the grafted cells, while they used autologous cells, the problem still exists and requires further optimization (Luciani et al., 2024).

Statistical Analysis

The ANOVA test was performed on BMS scores to compare the motor recovery of the patients. Further Tukey post hoc analysis ratified the significance in the iPSC and control group which was significant at day twenty-one and day twenty-eight post-injury ($p<0.05$). Image analysis performed using ImageJ software for lesion cavity size was reduced in the iPSC group by 35% compared to controls, $P < 0.01$. These results prove the research hypothesis that iPSC-derived cells enhance both the restoration of structure and function in SCI.

Safety Information

Following the application of iPSCs in treating spinal cord injury (SCI), several safety issues have been identified which should be considered to make iPSCs safe for use in clinical practice. One of the real concerns is the ability of

the iPSCs to form a tumor because of their potential to be dysregulated, especially if they have not fully differentiated before being grafted. Tingling of blood vessels and differentiation can occur resulting in teratomas which are benign tumors made up of many different types of tissue. Scientists are currently focusing large efforts on perfecting methods on ways to effectively dissociate iPSCs before transplantation to reduce this risk. Immune rejection is also an area of concern since autologous iPSCs can help minimize this problem, reprogramming and culturing cells for transplant may instigate the immune response anyway. Furthermore, forging the iPSC-derived cells into the defective spinal cord and their functional integration is vital to prevent undesirable sequelae such as cytoarchitectural dysfunction or inadequate tissue repair. Thirdly, little is known regarding the chronic effects of iPSCs' transplantation into spinal cord tissue, such as overactivation leading to unwanted electrical signaling, uncontrollable proliferation, or abnormal communications with other cells that form a part of the growing tissue. To overcome these issues much preclinical testing, safety checks, and supervision of clinical trials are required to determine the applicability and safety of iPSC-based therapeutic approaches for cervical SCI.

Discussion

Therefore, the results of this present research show compelling evidence in favor of the applicability of iPSC-derived NPCs in the treatment of SCI. The findings of the differentiated neurons, functional oligodendrocytes, and astrocytes in the lesion site indicate that the final exogenous source can be an important tool for both the replacement of lost neurons and supporting roles derived from glial cells for spinal cord repair. NeuN+ neuronal integration around the lesion periphery suggests that possible synaptic formation took place, which most probably contributed to the enhanced motor function of the affected limb. Furthermore, the presence of Olig2+ oligodendrocytes following axonal tracts at the periphery of lesions points to remyelination, which is indispensable for the regeneration of signal conveying across ischemic spinal networks (Suda, 2021).

The functional recovery found in BMS scores shows the potential of iPSC in achieving structural changes and its related movement functionalities. This study supports the observation made by Kajikawa et al. (2020) on the usefulness of iPSC-derived cells in rendering motor recovery by way of synaptic rewiring and remyelination. Nonetheless, MSCs only act as Paracrine signalers that modulate inflammation without directly differentiating into the neural lineage whereas, iPSC directly provides a replaced cell and therefore has a straight long-term functional advantage (Zeng et al., 2023).

From the present study, it can be concluded that iPSC-derived NPCs possess the potential for the treatment of SCI in the human Trail because they can offer structural and functional repair from different viewpoints. The enhanced motor function established in the experimental group confirms the reparative properties of iPSCs for potential application in SCI-affected patients. Furthermore, the differentiation into both nectinor and glial cell lineages delineates the complexity of spinal repair as both neuronal and glial cells are important in the CNS.

Nevertheless, certain issues persist Even given these positive results. The immune response seen even to such a degree indicates that working with iPSCs for therapy uses, even in autological cases, is not as simple as it may seem. Other works, including those from Luciani et al. (2024), propose that the reprogramming process may bring in epigenetic changes that activate the immune response. Some of these problems may be efficiently resolved with the help of gene-editing approaches or immune-compatible cell lines and, therefore, increase the safety of iPSC therapies. Moreover, although there were no tumors we also need further investigation to find the best techniques and parameters for the tumor-free clinical applications.

Conclusion

Therefore, this work reviews the application of iPSC-derived NPCs to show that they play an important role in both structural repair and functional motor recovery in SCI. Through the differentiation of neurons, oligodendrocytes, and astrocytes, the iPSCs contribute to spinal repair through cell replacement, generation of the myelin sheath, and regulation of inflammation. The enhancement of BMS noted in the studies points towards iPSCs' ability to convert structural repair into functional recovery making it a viable regenerative treatment for SCI.

However, immunological rejection and tumor formation are considerable drawbacks that have yet to be overcome, current improvements in the application of iPSCs— including genetic engineering and selection and differentiation techniques—may overcome these hurdles. This study provides a foundation for future descriptive, translational research involving iPSCs and sets the stage for future clinical trials. Last, one can conclude that iPSCs can be a useful line towards the development of personalized treatments for spinal cord injury which can help restore the functions and overall quality of life of affected patients.

This work thus establishes the feasibility of iPSC-derived neural progenitors for spinal cord repair with improvements in motor function and integration in experimental models of SCI While iPSC offers an advantage over ESCs by the ability to avoid immune rejection on autologous transplantation. However, problems associated with immune responses and tumor formation need to be overcome for broader usage in the clinic. Future investigations of this approach should concentrate on the optimization of differentiation processes, minimization of immune response, and assessment of clinical safety in further detail. Further improvements mean that iPSC-based treatments may be established as the fundamental strategy of spinal cord injury treatment for patients with severe motor disability.

Limitations and Future Directions

While results seem promising, there are several limitations to keep in mind. The first is that despite only a small percentage of cells integrating as expected in vitro when we performed immunohistochemistry this confirmed differentiation to neural lineages; functionally quantifying neuronal engraftment remains more difficult though. Electrophysiological recordings could be used in future studies to directly measure synapse formation between transplanted and host tissue. In addition, although in the current work cyclosporine treatment minimized immune rejection, to clinically translate this approach, immune tolerance must be achieved. iPSCs may be genetically modified to lower immunogenicity by knocking down HLA antigens, which comes with the potential of reducing or eliminating the need for immunosuppression (Matin et al., 2023).

Finally, iPSCs are still known for their possible tumorigenic profiles. No tumors were detected in this study, but future studies may evaluate iPSC-derived NPCs over longer periods to ensure their safety. Finally, mouse models are valuable but preliminary, and for proof of concept showing that iPSCs can be used to treat human SCI safely and effectively, they will have to be repeated in larger animal models with more complex spinal architectures.

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