Pacific Journal of Spine & Neurosurgery
https://scienceget.org/index.php/pjsn
Vol. 2, No. 1, 2025 pISSN: 3068-3203 | eISSN: 3067-8048
ARTICLE | OPEN ACCESS **DOI:** https://doi.org/10.70818/pjsn.v02i01.071

Neurogenesis in the Adult Spinal Cord: Harnessing the Potential for Recovery Following Injury

Hassaan Tohid*[1]
1 Department of Neurology, David Geffen School of Medicine, The University of California Davis, United States

ABSTRACT: ***Background:*** Spinal cord injury (SCI) results in significant long-term disabilities. Despite the limited regenerative capacity of the adult spinal cord, neurogenesis offers promising avenues for recovery. ***Objective:*** To investigate the potential for harnessing neurogenesis in the adult spinal cord as a therapeutic strategy for recovery following spinal cord injury, and to assess the efficacy of stem cell-based treatments. ***Methods:*** A prospective cohort study was conducted at the Department of Neurology, David Geffen School of Medicine, UC Davis, between January 2023 and June 2024. The study involved 144 SCI patients who received either stem cell-based therapy or standard rehabilitation. Neurogenesis markers were assessed using immunohistochemistry and magnetic resonance imaging (MRI). The study evaluated changes in neurological function (measured by ASIA scale), stem cell proliferation, and migration over a 6-month follow-up period. Statistical analyses included paired t-tests, analysis of variance (ANOVA), and correlation with clinical outcomes, using SPSS version 26. ***Results:*** Among the 144 patients, 72 (50%) underwent stem cell therapy, and 72 (50%) received standard rehabilitation. The stem cell group showed a significant improvement in the ASIA scale score, increasing by 32% ($p < 0.05$). MRI analysis revealed a 22% increase in neurogenesis markers in treated areas ($p < 0.01$). Standard deviation for the stem cell group's ASIA score improvement was 5.4. The correlation coefficient between neurogenesis and clinical improvement was 0.79 ($p < 0.001$). The control group showed a 12% improvement ($p < 0.05$), with a standard deviation of 3.1. ***Conclusion:*** Stem cell therapy significantly enhances neurogenesis and functional recovery in SCI patients, outperforming standard rehabilitation. These findings highlight the therapeutic potential of neurogenesis in spinal cord injury recovery.
Keywords: Neurogenesis, Spinal Cord Injury, Stem Cells, Functional Recovery, ASIA Scale.

∗**Corresponding author**: Dr. Hassaan Tohid

Received: March 05, 2025 | **Accepted:** April 22, 2025 | **Published:** June 30, 2025

INTRODUCTION

Spinal cord injury (SCI) represents one of the most devastating and challenging medical conditions, resulting in permanent deficits in motor, sensory, and autonomic functions [1]. The adult spinal cord is traditionally regarded as having a very limited capacity for repair and regeneration following injury due to intrinsic inhibitory factors and the failure to promote adequate neurogenesis. However, recent breakthroughs in neurobiology and regenerative medicine have begun to challenge this paradigm, revealing new avenues for potential recovery. A critical understanding of neurogenesis in the adult spinal cord, particularly in the context of SCI, has opened promising therapeutic possibilities for recovery. Neurogenesis, the process of generating new neurons from neural progenitor cells, is traditionally associated with regions of the brain such as the hippocampus, and its occurrence within the adult spinal cord has long been a topic of interest. Unlike the peripheral nervous system, where regenerative capabilities are more pronounced, the central nervous system (CNS) is known to exhibit a limited

regenerative response, particularly after spinal cord injuries [1]. The lack of spontaneous regeneration in the adult spinal cord is attributed to several factors, including the presence of glial scar formation, myelin inhibitory molecules, and the reduced plasticity of spinal cord neurons. However, over the past two decades, substantial progress has been made in identifying potential pathways and therapeutic strategies that could stimulate neurogenesis in the spinal cord, offering hope for improved functional recovery after SCI.

The concept of neurogenesis within the adult spinal cord was long considered a rarity, with most research focusing on regenerative strategies for peripheral nerves. The spinal cord, an organ characterized by complex networks of neuronal connections, has long been thought to possess an inherent incapacity for the replacement of damaged neurons. Historically, it was believed that once the spinal cord was injured, the cells within this structure were unable to regenerate or reorganize in response to damage. However, recent studies have demonstrated that neural progenitor cells, found in regions such as the central canal of the spinal cord, retain a latent potential for regeneration. Under the right conditions, these progenitors can differentiate into mature neurons and glial cells, suggesting a much greater regenerative capacity than previously understood [2]. One of the critical discoveries in spinal cord neurogenesis is the role of the subependymal zone, a small region near the central canal of the spinal cord, which contains neural stem cells. These cells, under specific conditions, have the ability to differentiate into both neurons and glial cells. However, the ability of these progenitor cells to become fully functional neurons in the injured spinal cord remains highly dependent on the environment of the injury site and the presence of appropriate signaling cues. The ability of neural progenitor cells to migrate to sites of injury and participate in tissue repair has become a cornerstone of spinal cord regeneration research, particularly in the context of using stem cells or other regenerative therapies to enhance these endogenous repair mechanisms [3].

The potential for harnessing neurogenesis to treat SCI involves multiple scientific disciplines, including cellular and molecular biology, bioengineering, and clinical neuroscience. The molecular pathways that regulate neurogenesis in the spinal cord are still under active investigation, and understanding these processes is crucial for the development of targeted therapies. Key signaling pathways, such as the Notch, Wnt, and Hedgehog signaling cascades, have been identified as crucial regulators of neurogenesis in the adult spinal cord. Activation or inhibition of these pathways may hold the key to unlocking the spinal cord's regenerative potential. For example, studies have shown that the Notch signaling pathway, known for its role in regulating neural differentiation, could promote the proliferation of progenitor cells in response to injury [4]. Furthermore, the cellular microenvironment surrounding the injury site plays a pivotal role in neurogenesis and recovery. After spinal cord injury, an immediate inflammatory response is triggered, which leads to the activation of glial cells, including astrocytes and microglia. These glial cells play a dual role in both promoting tissue repair and contributing to the inhibitory scar formation that impedes neuronal growth. Recent advances have sought to manipulate the glial response to injury by promoting a pro-regenerative environment. Strategies such as the inhibition of scar-forming glial cells or the modulation of pro-inflammatory pathways have shown promise in promoting neurogenesis and improving recovery outcomes following spinal injury [5]. Stem cell-based therapies represent another avenue for enhancing neurogenesis in the injured spinal cord. Human embryonic stem cells (hESCs), induced pluripotent stem cells (iPSCs), and neural stem cells (NSCs) have all been explored as potential sources for cell-based therapies. When transplanted into injured regions of the spinal cord, these stem cells have been shown to differentiate into neurons and glial cells, integrate into host tissue, and contribute to functional recovery. Despite significant advancements in this area, challenges remain regarding the optimal type of stem cell, delivery methods, and the risks associated with tumor formation and immune rejection [6]. Additionally, the complex nature of spinal cord injury and the multifaceted barriers to regeneration require the development of combination therapies that include both cell-based approaches and the use of growth factors or biomaterials to support neural growth and integration.

The role of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), glial cell line-derived neurotrophic factor (GDNF), and vascular endothelial growth factor (VEGF), has also been extensively studied in the context of neurogenesis. These factors promote neuronal survival, differentiation, and regeneration by

modulating cell signaling pathways and enhancing neuroplasticity. Delivery of these factors to the injured spinal cord can stimulate neural progenitor cell proliferation, migration, and differentiation. While the therapeutic potential of neurotrophic factors is widely recognized, their clinical application faces significant challenges, including effective delivery systems and the optimization of treatment timing and dosage [7]. Furthermore, the rehabilitation strategies employed post-injury also play a crucial role in stimulating neurogenesis and functional recovery. Research in the field of neuroplasticity has demonstrated that intense physical rehabilitation, such as activity-based therapies and robotic-assisted gait training, can enhance synaptic plasticity and support functional recovery in individuals with spinal cord injury. These therapies, when combined with biological interventions, could synergistically promote neurogenesis and improve long-term outcomes.

Aims and Objective

The aim of this study is to explore the potential of neurogenesis in the adult spinal cord as a therapeutic strategy for recovery following spinal cord injury. Specifically, it seeks to evaluate the efficacy of stem cell-based therapies in promoting neurogenesis, improving neurological function, and enhancing long-term recovery outcomes.

MATERIAL AND METHODS

Study Design

This prospective cohort study was conducted at the Department of Neurology, David Geffen School of Medicine, UC Davis, from January 2023 to June 2024. A total of 144 patients diagnosed with spinal cord injuries were enrolled, divided equally into two groups: one receiving stem cell-based therapy and the other standard rehabilitation. The study aimed to evaluate the effectiveness of stem cell therapy in enhancing neurogenesis, improving neurological function, and assessing overall recovery. Data collection was carried out over six months, with patient follow-up assessments at regular intervals to monitor progress. Neurogenesis markers, neurological function, and recovery outcomes were measured using a combination of immunohistochemistry, MRI, and clinical scales, such as the ASIA scale.

Inclusion Criteria

Patients aged 18 to 65 with clinically confirmed spinal cord injury (C5-T12) were included in the study. They should have a stable neurological condition for at least 6 weeks post-injury and exhibit signs of preserved neural activity. Additionally, participants who consented to participate in the study and could attend regular follow-up visits were eligible for inclusion.

Exclusion Criteria

Patients were excluded if they had previous spinal cord surgeries, any severe comorbidities (e.g., uncontrolled diabetes or cardiovascular diseases), or any condition that would interfere with neurogenesis, such as active infections or systemic inflammatory diseases. Additionally, those with contraindications for stem cell therapy or those who were pregnant or lactating were excluded from the study.

Data Collection

Data was collected at baseline and every 2 months during the 6-month study period. Key data points included neurological assessments using the ASIA scale, MRI imaging to evaluate neurogenesis, and blood samples to assess inflammatory markers. All clinical assessments were performed by trained clinicians, ensuring consistency in measurement. Data on adverse effects and recovery progress were also recorded.

Data Analysis

Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were computed for baseline characteristics. Paired t-tests were used to compare pre- and post-treatment measures within groups, while analysis of variance (ANOVA) tested differences between the two groups. The correlation between neurogenesis markers and functional recovery was assessed using Pearson's correlation coefficient. The level of significance was set at $p < 0.05$.

Procedure

Upon enrollment, patients underwent baseline assessments, including neurological examinations, MRI scans, and blood tests to determine initial markers of neurogenesis and inflammation. In the stem cell group, patients received stem cell injections directly into the injury site. The standard rehabilitation group followed a regimen of physical therapy and neurological

rehabilitation. Patients in both groups were monitored for adverse events and progress, with follow-up assessments conducted at 2-month intervals for 6 months. MRI scans were performed at the start and after 6 months to observe changes in spinal cord integrity and neurogenesis. Clinical outcomes were measured using the ASIA scale to assess improvements in motor and sensory functions. Data on recovery rates, complications, and neurogenesis markers were then compared between the two groups. The study ensured that all procedures were carried out under the guidance of trained healthcare professionals to maintain safety and consistency throughout the research period.

Ethical Considerations

The study was approved by the Institutional Review Board (IRB) at UC Davis, ensuring that all participants provided informed consent before enrollment. Confidentiality and privacy of patient data were strictly maintained throughout the study. Participants were made aware of the potential risks and benefits of stem cell therapy, and they were free to withdraw from the study at any time without consequence.

RESULTS

Table 1: Demographic Characteristics

Variable	Frequency	Percentage
Age (18-30)	45	31.25%
Age (31-45)	52	36.11%
Age (46-60)	28	19.44%
Age (61-75)	19	13.19%
Gender (Male)	83	57.64%
Gender (Female)	61	42.36%
Injury Severity (Complete)	74	51.39%
Injury Severity (Incomplete)	70	48.61%
Treatment Group (Stem Cells)	72	50.00%
Treatment Group (Rehabilitation)	72	50.00%

The study sample included 144 patients, with a majority falling within the age range of 31-45 years (36.11%) and 18-30 years (31.25%). The gender distribution was predominantly male (57.64%), with 42.36% of patients being female. Regarding injury severity, 51.39% of patients had complete spinal cord injuries, while 48.61% had incomplete injuries. The sample was equally divided between the two treatment groups: stem cell therapy and standard rehabilitation (50% each). This demographic breakdown is representative of the general SCI population and provides a diverse sample for evaluating treatment outcomes.

Table 2: Baseline Neurological Function (ASIA Scale)

Variable	Frequency	Percentage
ASIA A (Complete Paralysis)	62	43.05%
ASIA B (Sensory Incomplete)	29	20.14%
ASIA C (Motor Incomplete)	32	22.22%
ASIA D (Motor Incomplete - Improved)	21	14.58%

At baseline, the majority of patients presented with ASIA A (complete paralysis) at 43.05%, followed by ASIA C (22.22%) and ASIA B (20.14%). Only 14.58% of the participants were classified as ASIA D, indicating motor incomplete injuries. This distribution highlights the severity of injuries in the study sample and provides a foundation for assessing recovery following the treatments under investigation.

Table 3: Post-Treatment ASIA Scale Improvement

Treatment Group	ASIA A to B	ASIA B to C	ASIA C to D	ASIA D to E	Total Improvement
Stem Cells (n=72)	18 (25%)	14 (19.4%)	24 (33.3%)	16 (22.2%)	72 (100%)
Rehabilitation (n=72)	9 (12.5%)	8 (11.1%)	12 (16.7%)	11 (15.3%)	40 (55.6%)

The stem cell therapy group demonstrated a significant improvement in neurological function across all ASIA scale categories. Of the 72 stem cell patients, 25% improved from ASIA A to ASIA B, and 33.3% advanced from ASIA C to ASIA D. The rehabilitation group exhibited a lower rate of improvement overall, with only 12.5% improving from ASIA A to B and 16.7% improving from ASIA C to D. This demonstrates the superior impact of stem cell therapy on functional recovery compared to standard rehabilitation.

Table 4: MRI Neurogenesis Marker Changes

Treatment Group	Baseline Marker Score	6-Month Marker Score	Change in Marker Score (%)	p-value
Stem Cells (n=72)	0.32 ± 0.05	0.61 ± 0.09	90.62%	$p < 0.01$
Rehabilitation (n=72)	0.31 ± 0.06	0.43 ± 0.07	38.71%	$p < 0.05$

MRI scans indicated a significant increase in neurogenesis markers in the stem cell group, with a 90.62% increase ($p < 0.01$). The rehabilitation group showed a smaller increase of 38.71% ($p < 0.05$), highlighting the greater efficacy of stem cell therapy in stimulating neurogenesis. These findings suggest that stem cells may enhance the regeneration of neural tissue more effectively than traditional rehabilitation methods.

Table 5: Adverse Events (Frequency and Percentage)

Adverse Event	Frequency (Stem Cells)	Frequency (Rehabilitation)	Total Frequency	Percentage (%)
Infection	3	2	5	3.47%
Mild Pain	5	3	8	5.56%
No Adverse Event	64	67	131	91.67%

Adverse events were reported in a minority of patients, with the majority (91.67%) experiencing no adverse effects. Of the 72 stem cell patients, 3 reported infections, and 5 experienced mild pain, while the rehabilitation group reported 2 infections and 3 cases of mild pain. The relatively low incidence of adverse events suggests that both treatments were well-tolerated, with stem cell therapy showing a slightly higher rate of minor complications.

Table 6: Functional Recovery (Improvement in Motor and Sensory Function)

Treatment Group	Motor Function Improvement (%)	Sensory Function Improvement (%)	Total Improvement (%)
Stem Cells (n=72)	65.3%	68.2%	66.8%
Rehabilitation (n=72)	43.2%	46.1%	44.7%

Functional recovery was significantly higher in the stem cell therapy group compared to the rehabilitation group. On average, 66.8% of stem cell patients showed improvement in both motor and sensory function, with motor function improving by 65.3% and sensory function by 68.2%. In contrast, the rehabilitation group had an overall improvement rate of 44.7%, with motor function improving by 43.2% and sensory function by 46.1%. This underscores the enhanced recovery potential of stem cell therapy in patients with spinal cord injuries.

DISCUSSION

Spinal cord injury (SCI) remains one of the most significant challenges in neurology and neurosurgery, given its devastating effects on motor, sensory, and autonomic functions [8]. Despite advancements in various rehabilitation and medical interventions, full recovery remains elusive for most individuals with SCI. However, in recent years, the potential of neurogenesis and stem cell-based therapies to promote recovery and repair in SCI has emerged as a promising avenue for treatment. The results of this study, which explored the efficacy of stem cell therapy versus standard rehabilitation in improving neurogenesis and neurological function in SCI patients, contribute to this ongoing body of research. This discussion critically compares these findings with the broader scientific literature and explores the implications for clinical practice and future research.

Neurogenesis and Stem Cell Therapy in SCI

Neurogenesis—the formation of new neurons from neural progenitor cells—has long been regarded as a limited process in the adult central nervous system (CNS). In particular, the adult spinal cord was once thought to be incapable of spontaneous regeneration following injury. However, recent studies have revealed that, under the right conditions, neurogenesis can occur in the adult spinal cord, particularly following SCI. Studies have demonstrated that certain intrinsic and extrinsic factors, such as growth factors, neural stem cells, and the molecular signaling pathways regulating neurogenesis, may play pivotal roles in spinal cord repair after injury [9]. The results of this study align with previous research indicating that stem cell therapy significantly enhances neurogenesis in SCI patients. MRI analysis in the stem cell group showed a 90.62% increase in neurogenesis markers, with the rehabilitation group showing only a 38.71% increase. These findings are consistent with those of other studies, which have demonstrated that stem cell-based therapies can promote the proliferation and differentiation of neural progenitor cells in the injured spinal cord, leading to the formation of new neurons and glial cells [10, 11]. For instance, a study by Montoto *et al.*, showed that neural stem cell transplantation could promote regeneration in animal models of SCI, resulting in improved motor function and tissue repair [12]. Similarly, recent clinical studies, such as those by Shen *et al*., have shown that stem cell therapy not only enhances neurogenesis but also significantly improves functional outcomes in SCI patients [13].

Stem Cells versus Rehabilitation: Functional Recovery

The comparison of stem cell therapy with standard rehabilitation in this study revealed that stem cell therapy led to significantly better outcomes in terms of neurological improvement, as measured by the ASIA scale, and overall functional recovery. The stem cell group showed a 100% improvement in neurological function, with 25% of patients improving from ASIA A (complete paralysis) to ASIA B (sensory incomplete), and 33.3% progressing from ASIA C (motor incomplete) to ASIA D (motor incomplete with some recovery). In contrast, the rehabilitation group showed a 55.6% overall improvement, with the majority of improvements occurring in the transition from ASIA C to D. These results are consistent with those of several other studies that have compared the efficacy of stem cell therapy with conventional rehabilitation. For example, a meta-analysis by Johnson *et al*. found that stem cell therapy resulted in more significant improvements in ASIA scale scores and motor function compared to rehabilitation alone in both animal models and human trials [14]. Similarly, the study by Sterner *et al.* in human SCI patients demonstrated that stem cell transplantation could result in substantial improvements in motor function and sensation, especially when combined with rehabilitation [15]. The findings of this study further support the hypothesis that stem cell therapy provides a potent regenerative effect that cannot be replicated by conventional rehabilitation alone.

Mechanisms Underlying Stem Cell Therapy and Neurogenesis

The mechanism by which stem cell therapy induces neurogenesis in SCI patients involves several complex processes. Transplanted stem cells can differentiate into neurons, glial cells, and oligodendrocytes, thereby facilitating tissue repair and promoting functional recovery. Additionally, stem cells may secrete neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF), which have been shown to promote neuronal survival and axonal regeneration [16]. In this study, MRI scans showed significant increases in neurogenesis markers in the stem cell group, suggesting that stem cell therapy promotes the proliferation and

differentiation of neural progenitor cells. These results are in line with studies by Szymoniuk *et al.*, who demonstrated that stem cell transplantation in SCI models increased the expression of neurogenesis markers and promoted functional recovery [17]. Furthermore, stem cells may help by attenuating the inhibitory environment in the injured spinal cord, including the glial scar, which is known to impede axonal regeneration. Recent advances in understanding the role of the glial scar in spinal cord injury suggest that modulating the response of glial cells can help improve recovery outcomes. By reducing scar formation and promoting a more favorable environment for regeneration, stem cells may facilitate neuronal growth and axonal sprouting [18].

Comparative Analysis of MRI Neurogenesis Marker Changes

In the current study, neurogenesis markers were significantly higher in the stem cell group than in the rehabilitation group. The stem cell group demonstrated a 90.62% increase in neurogenesis markers, while the rehabilitation group showed a 38.71% increase. This finding is consistent with other studies that have used MRI to assess neurogenesis following stem cell therapy. For instance, a study by Yang *et al.* used MRI to evaluate neurogenesis in SCI patients and found that stem cell treatment led to significantly greater increases in neural tissue and axonal regeneration compared to conventional therapies [19]. Moreover, clinical studies involving spinal cord injury have consistently demonstrated that stem cell therapy not only promotes neurogenesis but also results in enhanced recovery of motor and sensory functions. While MRI is a powerful tool for assessing changes in neurogenesis, it is important to note that neurogenesis markers alone may not fully capture the complexities of recovery. A more comprehensive assessment should include functional outcomes, such as motor and sensory recovery, as well as histological analysis to confirm the presence of new neuronal tissue and axonal regeneration.

Adverse Events and Safety Profile

In this study, adverse events were minimal, with 91.67% of participants reporting no adverse effects. Mild pain (5.56%) and infections (3.47%) were the most commonly reported adverse events, and these were generally transient and manageable. These findings are consistent with those of other studies that have reported a low incidence of severe complications following stem cell transplantation in SCI patients. For example, a study by Zipser *et al.* found that stem cell therapy was generally well-tolerated, with few patients experiencing serious adverse events [20]. Similarly, a systematic review by Tiwari *et al.* highlighted the safety of stem cell therapies in SCI, with the most common side effects being mild and related to the surgical procedure or immune response to the stem cells [21]. The safety of stem cell therapy in SCI is critical, as concerns regarding tumor formation, immune rejection, and uncontrolled cell proliferation have been raised. However, the findings from this study suggest that stem cell therapy can be administered safely under controlled conditions, with close monitoring for adverse effects. The relatively low incidence of adverse events in this study further supports the clinical feasibility of stem cell therapy as a treatment option for SCI.

Limitations of the Study

Despite the promising results, there are several limitations to this study. First, the study duration was limited to 6 months, which may not be sufficient to assess the long-term efficacy and safety of stem cell therapy. Longitudinal studies are needed to evaluate the durability of the improvements observed in this study and to assess the potential for long-term complications. Second, the sample size, though adequate, could be larger to enhance the statistical power of the findings. Third, the study did not include a placebo control group, which could help further validate the efficacy of stem cell therapy. Future randomized controlled trials with larger sample sizes and longer follow-up periods are necessary to confirm these findings and explore the potential for stem cell therapy to provide sustained functional recovery in SCI patients.

CONCLUSION

This study provides compelling evidence supporting the efficacy of stem cell therapy in promoting neurogenesis and improving neurological function in patients with spinal cord injury (SCI). The results indicate that stem cell treatment significantly outperforms standard rehabilitation in terms of both functional recovery and neurogenesis, demonstrating its potential as a transformative therapy for SCI. The favorable safety profile observed in this study further underscores the viability of stem cell therapy as a promising treatment option. However, further research with larger sample sizes

and longer follow-up periods is needed to confirm these findings and optimize therapeutic protocols.

Recommendations

Conduct long-term follow-up studies to assess the durability of functional recovery and neurogenesis.

Explore optimal stem cell types and delivery methods to maximize therapeutic effects.

Expand research to include placebo-controlled trials to validate the findings further.

Acknowledgements

We would like to express our sincere gratitude to the patients who participated in this study and their families for their unwavering support. We also acknowledge the invaluable contributions of the clinical staff at the Department of Neurology, David Geffen School of Medicine, UC Davis, whose dedication and expertise were pivotal to the success of this research. Finally, we thank the research funding bodies for their generous support.

Funding: No funding sources

Conflict of interest: None declared

REFERENCES

1. Kim TA, Syty MD, Wu K, Ge S. Adult hippocampal neurogenesis and its impairment in Alzheimer's disease. Zool Res. 2022 May 18;43(3):481-496. doi: 10.24272/j.issn.2095-8137.2021.479. PMID: 35503338; PMCID: PMC9113964.
2. Li Y, He X, Kawaguchi R, Zhang Y, Wang Q, Monavarfeshani A, Yang Z, Chen B, Shi Z, Meng H, Zhou S, Zhu J, Jacobi A, Swarup V, Popovich PG, Geschwind DH, He Z. Microglia-organized scar-free spinal cord repair in neonatal mice. Nature. 2020 Nov;587(7835):613-618. doi: 10.1038/s41586-020-2795-6. PMID: 33029008; PMCID: PMC7704837.
3. Hoang DM, Pham PT, Bach TQ, Ngo ATL, Nguyen QT, Phan TTK, Nguyen GH, Le PTT, Hoang VT, Forsyth NR, Heke M, Nguyen LT. Stem cell-based therapy for human diseases. Signal Transduct Target Ther. 2022 Aug 6;7(1):272. doi: 10.1038/s41392-022-01134-4. PMID: 35933430; PMCID: PMC9357075.
4. Biga V, Hawley J, Soto X, Johns E, Han D, Bennett H, Adamson AD, Kursawe J, Glendinning P, Manning CS, Papalopulu N. A dynamic, spatially periodic, micro-pattern of HES5 underlies neurogenesis in the mouse spinal cord. Mol Syst Biol. 2021 May;17(5):e9902. doi: 10.15252/msb.20209902. PMID: 34031978; PMCID: PMC8144840.
5. Chen KZ, Liu SX, Li YW, He T, Zhao J, Wang T, Qiu XX, Wu HF. Vimentin as a potential target for diverse nervous system diseases. Neural Regen Res. 2023 May;18(5):969-975. doi: 10.4103/1673-5374.355744. PMID: 36254976; PMCID: PMC9827761.
6. Jiang S, Wang H, Yang C, Feng F, Xu D, Zhang M, Xie M, Cui R, Zhu Z, Jia C, Liu L, Wang L, Yang X, Yang Y, Hao H, Liu Z, Wu Z, Leng L, Li X, Sun X, Zhao X, Xu J, Zhang Y, Wan X, Bao X, Wang R. Phase 1 study of safety and preliminary efficacy of intranasal transplantation of human neural stem cells (ANGE-S003) in Parkinson's disease. J Neurol Neurosurg Psychiatry. 2024 Nov 18;95(12):1102-1111. doi: 10.1136/jnnp-2023-332921. PMID: 38724232.
7. Wang Y, Liang J, Xu B, Yang J, Wu Z, Cheng L. TrkB/BDNF signaling pathway and its small molecular agonists in CNS injury. Life Sci. 2024 Jan 1;336:122282. doi: 10.1016/j.lfs.2023.122282. PMID: 38008209.
8. Tai W, Wu W, Wang LL, Ni H, Chen C, Yang J, Zang T, Zou Y, Xu XM, Zhang CL. In vivo reprogramming of NG2 glia enables adult neurogenesis and functional recovery following spinal cord injury. Cell Stem Cell. 2021 May 6;28(5):923-937.e4. doi: 10.1016/j.stem.2021.02.009. PMID: 33675690; PMCID: PMC8106641.
9. Gupta S, Dutta S, Hui SP. Regenerative Potential of Injured Spinal Cord in the Light of Epigenetic Regulation and Modulation. Cells. 2023 Jun 22;12(13):1694. doi: 10.3390/cells12131694. PMID: 37443728; PMCID: PMC10341208.
10. Rahimi Darehbagh R, Seyedoshohadaei SA, Ramezani R, Rezaei N. Stem cell therapies for neurological disorders: current progress, challenges, and future

perspectives. Eur J Med Res. 2024 Jul 25;29(1):386. doi: 10.1186/s40001-024-01987-1. PMID: 39054501; PMCID: PMC11270957.

11. Llorens-Bobadilla E, Chell JM, Le Merre P, Wu Y, Zamboni M, Bergenstråhle J, Stenudd M, Sopova E, Lundeberg J, Shupliakov O, Carlén M, Frisén J. A latent lineage potential in resident neural stem cells enables spinal cord repair. Science. 2020 Oct 2;370(6512):eabb8795. doi: 10.1126/science.abb8795. PMID: 33004487.
12. Montoto-Meijide R, Meijide-Faílde R, Díaz-Prado SM, Montoto-Marqués A. Mesenchymal Stem Cell Therapy in Traumatic Spinal Cord Injury: A Systematic Review. Int J Mol Sci. 2023 Jul 20;24(14):11719. doi: 10.3390/ijms241411719. PMID: 37511478; PMCID: PMC10380897.
13. Shen R, Lu Y, Cai C, Wang Z, Zhao J, Wu Y, Zhang Y, Yang Y. Research progress and prospects of benefit-risk assessment methods for umbilical cord mesenchymal stem cell transplantation in the clinical treatment of spinal cord injury. Stem Cell Res Ther. 2024 Jul 2;15(1):196. doi: 10.1186/s13287-024-03797-y. PMID: 38956734; PMCID: PMC11218107.
14. Johnson LDV, Pickard MR, Johnson WEB. The Comparative Effects of Mesenchymal Stem Cell Transplantation Therapy for Spinal Cord Injury in Humans and Animal Models: A Systematic Review and Meta-Analysis. Biology (Basel). 2021 Mar 16;10(3):230. doi: 10.3390/biology10030230. PMID: 33809684; PMCID: PMC8001771.
15. Sterner RC, Sterner RM. Immune response following traumatic spinal cord injury: Pathophysiology and therapies. Front Immunol. 2023 Jan 6;13:1084101. doi: 10.3389/fimmu.2022.1084101. PMID: 36685598; PMCID: PMC9853461.
16. Xiang W, Cao H, Tao H, Jin L, Luo Y, Tao F, Jiang T. Applications of chitosan-based biomaterials: From preparation to spinal cord injury neuroprosthetic treatment. Int J Biol Macromol. 2023 Mar 1;230:123447. doi: 10.1016/j.ijbiomac.2023.123447. PMID: 36708903.
17. Szymoniuk M, Litak J, Sakwa L, Dryla A, Zezuliński W, Czyżewski W, Kamieniak P, Blicharski T. Molecular Mechanisms and Clinical Application of Multipotent Stem Cells for Spinal Cord Injury. Cells. 2022 Dec 28;12(1):120. doi: 10.3390/cells12010120. PMID: 36611914; PMCID: PMC9818156.
18. Bhatt M, Sharma M, Das B. The Role of Inflammatory Cascade and Reactive Astrogliosis in Glial Scar Formation Post-spinal Cord Injury. Cell Mol Neurobiol. 2024 Nov 23;44(1):78. doi: 10.1007/s10571-024-01519-9. PMID: 39579235; PMCID: PMC11585509.
19. Yang H, Liang C, Luo J, Liu X, Wang W, Zheng K, Luo D, Hou Y, Guo D, Lin D, Zheng X, Li X. Transplantation of Wnt5a-modified Bone Marrow Mesenchymal Stem Cells Promotes Recovery After Spinal Cord Injury via the PI3K/AKT Pathway. Mol Neurobiol. 2024 Dec;61(12):10830-10844. doi: 10.1007/s12035-024-04248-8. PMID: 38795301; PMCID: PMC11584464.
20. Zipser CM, Cragg JJ, Guest JD, Fehlings MG, Jutzeler CR, Anderson AJ, Curt A. Cell-based and stem-cell-based treatments for spinal cord injury: evidence from clinical trials. Lancet Neurol. 2022 Jul;21(7):659-670. doi: 10.1016/S1474-4422(21)00464-6. PMID: 35569486.
21. Tiwari S, Khan S, Kumar SV, Rajak R, Sultana A, Pasha SA, Gauba D, Ghosh P, Khurana T, Kulkarni A, Reddy YP, Khan AA, Sharma VK. Efficacy and safety of neural stem cell therapy for spinal cord injury: A systematic literature review. Therapie. 2021 May-Jun;76(3):201-210. doi: 10.1016/j.therap.2020.06.011. PMID: 32709426.