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Advances of the PI3K/AKT/mTOR Pathway in the Neural Repair of Spinal Cord Injury

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Abstract: ***Spinal cord injury (SCI) induces catastrophic neurological deficits, activating multiple signaling pathways, notably the phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT)/mechanistic target of rapamycin (mTOR) pathway. Current treatments primarily offer symptomatic relief without addressing underlying pathophysiology. Emerging research highlights the PI3K/AKT/mTOR pathway's crucial role in regulating neuronal survival, axon regeneration, glial responses, autophagy, and immune modulation post-SCI. Modulating this pathway post-injury shows promise in reducing inflammation, apoptosis, and neuropathic pain, while promoting neural repair. Given its central role, the PI3K/AKT/mTOR pathway is identified as a key therapeutic target for SCI management. This review summarizes current knowledge on SCI pathology, details the PI3K/AKT/mTOR pathway's characteristics, and explores its dual roles in pathology and therapeutic interventions, aiming to provide a comprehensive reference for future SCI research and targeted therapies.***

Keywords: PI3K/AKT/mTOR signaling pathway, Spinal cord injury, Neural repair, Inflammation.

1. Introduction

Spinal cord injury (SCI) is a catastrophic neurological condition that produces lasting motor, sensory and autonomic deficits, imposing profound personal and socioeconomic burdens worldwide. Recent global estimates indicate hundreds of thousands of new cases annually and millions living with chronic SCI, with substantial variation by region, mechanism and age group [1]. Primary injury causes immediate tissue disruption, hemorrhage and cell necrosis at the lesion epicenter. Secondary injury mechanisms — ischemia, excitotoxicity, oxidative stress, blood–spinal-cord barrier breakdown, neuroinflammation, oligodendrocyte loss, demyelination and apoptosis—then propagate tissue damage over hours to weeks, producing a hostile microenvironment that limits axonal regrowth and functional recovery [2]. Modern research has emphasized mechanistic dissection of intracellular signaling networks that govern neuronal survival, axon growth, inflammation and glial responses [3]. Major signaling modules implicated in SCI repair include Mitogen-activated protein kinase (MAPK), Janus kinase/signal transducer and activator of transcription (JAK/STAT), Wnt/β-catenin, RhoA/Rho-associated coiled-coil-forming protein kinase (ROCK) and the phosphoinositide 3-kinase (PI3K)/AKT/mechanistic target of rapamycin (mTOR) axis. Activation of PI3K catalyzes generation of phosphatidylinositol (3,4,5)-trisphosphate, recruiting and activating AKT; downstream, AKT modulates multiple substrates including mTOR complexes (mTORC1/2), glycogen synthase kinase-3β (GSK3β), Bcl-2 family members and components of the autophagy machinery [4]. Through these effectors, PI3K/AKT/mTOR signaling can inhibit apoptosis, reduce oxidative stress, regulate autophagy flux, and enhance axon growth capacity—properties that have attracted extensive interest as therapeutic entry points for SCI [5]. In this review we summarize the key pathological mechanisms that create barriers to repair, then critically review current knowledge of PI3K/AKT/mTOR involvement in neuronal survival, axon regeneration, glial responses, autophagy and immune modulation after SCI.

2. Literature Search Strategy

We conducted a comprehensive literature search using three major scientific databases—PubMed, Web of Science, and EMBASE. Search strategies incorporated the key terms "spinal cord injury," "PI3K/AKT/mTOR signaling pathway," and "neuroprotection." Relevant publications addressing the pathophysiology of SCI, post-injury immune responses, and the regulatory role of the PI3K/AKT/mTOR pathway were systematically evaluated. To ensure the accuracy and relevance of the evidence base, studies that were outdated, duplicated, or methodologically weak were carefully excluded through a rigorous screening process.

3. Pathology and Signaling Pathway of SCI

SCI initiates a complex and dynamic pathological process that unfolds in two major phases: primary and secondary injury. Early after trauma, excitotoxicity driven by excessive glutamate release and ionic imbalance leads to calcium overload and mitochondrial dysfunction. The production of reactive oxygen and nitrogen species causes oxidative stress, damaging membranes, proteins, and DNA. At the same time, breakdown of the blood–spinal cord barrier permits infiltration of peripheral immune cells, while resident microglia and astrocytes become activated. Although inflammatory signaling helps clear debris, excessive or prolonged inflammation contributes to neuronal apoptosis, demyelination, and axonal degeneration. As the injury evolves, astrocytes proliferate and form the glial scar; this structure stabilizes the lesion environment but imposes a physical and biochemical barrier to axonal regeneration through deposition of inhibitory extracellular matrix molecules [6]. Current research has increasingly focused on intracellular signaling pathways that regulate neuronal survival, inflammation, and regenerative capacity. The MAPK pathway is a key modulator of stress responses, inflammation, and apoptosis. Its dysregulation after SCI contributes to neuronal death and glial activation. The JAK/STAT pathway plays a pivotal role in immune and

inflammatory signaling. Activation of STAT3 in astrocytes is essential for glial scar formation, while in neurons it can promote survival. The Wnt/β-catenin pathway influences neurogenesis, axonal growth, and tissue patterning. After SCI, altered Wnt signaling affects both regenerative responses and inflammatory activation. The RhoA/ROCK pathway is a central inhibitor of cytoskeletal dynamics and axon extension. Its post-injury activation contributes to growth cone collapse, demyelination, and scar-associated inhibition. The PI3K/AKT/mTOR pathway regulates cell survival, protein synthesis, autophagy, and intrinsic axon growth capacity [7]. Together, these signaling pathways represent major research hotspots, offering promising therapeutic targets for reducing secondary injury and promoting neural repair following SCI.

4. The PI3K/AKT/mTOR Signaling Pathway

The PI3K/AKT/mTOR axis is a conserved intracellular signaling cascade that integrates extracellular growth factors, trophic signals, energy status and stress cues to regulate cell survival, metabolism, protein synthesis, cytoskeletal dynamics and autophagy. Canonically, receptor tyrosine kinases (RTKs) or G-protein–coupled receptors activate class I phosphoinositide 3-kinases (PI3Ks), generating phosphatidylinositol-3,4,5-trisphosphate (PIP_3). PIP_3 recruits and activates AKT (protein kinase B) at the plasma membrane; activated AKT phosphorylates numerous substrates including TSC2 and GSK-3β, relieving inhibition of the mechanistic target of rapamycin (mTOR). mTOR functions within two distinct complexes: mTORC1 (regulates cap-dependent translation, ribosome biogenesis and autophagy via ULK1) and mTORC2 (controls cytoskeletal organization and phosphorylates AKT on Ser473, forming a feedback loop). Negative regulation is exerted principally by the lipid phosphatase PTEN, which dephosphorylates PIP_3 and limits AKT activation [8]. Recent research has highlighted the pathway's significance across a broad range of diseases. In oncology, PI3K/AKT/mTOR hyperactivation drives tumor proliferation, angiogenesis, metabolic reprogramming, and treatment resistance; thus, PI3K and mTOR inhibitors have become major therapeutic strategies [9]. In metabolic disorders such as type 2 diabetes and obesity, dysregulation of AKT signaling impairs insulin sensitivity and glucose homeostasis. Neurodegenerative diseases, including Alzheimer's and Parkinson's, have been linked to altered mTOR-dependent autophagy, influencing protein aggregation and neuronal survival. Cardiovascular research shows that abnormal PI3K/AKT activity contributes to myocardial hypertrophy, ischemia-reperfusion injury, and vascular dysfunction. In immune-mediated diseases, the pathway modulates lymphocyte activation and inflammatory cytokine signaling [10]. Within the field of SCI, the PI3K/AKT/mTOR pathway has emerged as a major therapeutic focus. Post-injury activation of this cascade promotes neuronal survival, inhibits apoptosis, supports axonal regeneration, and regulates autophagy—key processes for neural repair. Modulating PI3K/AKT/mTOR signaling, whether through pharmacological agents, gene regulation, or biomaterial-based delivery, is now considered one of the most promising strategies for enhancing neuroprotection and functional recovery after SCI.

5. Roles of the PI3K/AKT/mTOR Signaling Pathway in SCI

5.1 Promoting Axonal Regeneration and Myelin Formation

A primary barrier to functional recovery after SCI is the limited intrinsic growth capacity of mature CNS neurons and the inhibitory extracellular milieu. Activation of PI3K/AKT/mTOR enhances neuronal growth programs by increasing protein synthesis, cytoskeletal remodeling, and axonal transport, and it counteracts intrinsic suppressors such as PTEN. Biomaterial-based and gene-therapy approaches exploit this principle to drive axonal extension beyond lesion sites. For instance, forced upregulation of a hyperactive PI3Kδ isoform in adult corticospinal neurons elevated downstream pS6 signaling and enabled long-distance corticospinal tract regeneration with behavioral improvements [11]. Constitutively active AKT3 expression likewise promoted corticospinal regeneration and sprouting, underscoring the potency of this pathway in restoring neuron-intrinsic growth capacity, although excessive activation may pose safety concerns such as seizure susceptibility [12]. Beyond axons, PI3K/AKT/mTOR signaling is increasingly appreciated as a regulator of oligodendrocyte lineage maturation and remyelination. Fucoidan treatment promoted oligodendrocyte precursor cell (OPC) differentiation into mature oligodendrocytes via PI3K/AKT/mTOR activation, improving myelin ultrastructure and locomotor outcomes [13]. A related strategy used Neuregulin-1 to transdifferentiate reactive astrocytes toward an oligodendrocyte lineage, an effect mediated by PI3K/AKT/mTOR upregulation, resulting in enhanced remyelination and axonal protection in vivo [14]. Combination rehabilitation approaches further support the pathway's role in myelin preservation; bone marrow mesenchymal stem cell (BMMSC) transplantation coupled with exercise activated PI3K/AKT/mTOR, reduced scar burden, and enhanced axon-myelin integrity [15]. Collectively, these studies position PI3K/AKT/mTOR as a key molecular lever for both axonal regeneration and re-establishment of myelinated tracts after SCI.

5.2 Inhibiting Neuronal Apoptosis and Promoting Cell Survival

Neuronal and glial apoptosis contribute substantially to secondary injury pathology. Activation of the PI3K/AKT/mTOR signaling pathway promotes cell survival primarily by suppressing pro-apoptotic signaling pathways, such as Bax-mediated mitochondrial dysfunction and caspase activation, while concomitantly upregulating anti-apoptotic proteins, including Bcl-2. Multiple interventions show reduced neuronal death when this pathway is appropriately engaged. For example, magnetic nanoparticle-based NSC delivery systems improved neuronal survival and reduced apoptosis, with PI3K/AKT/mTOR activation linked to enhanced NSC neuronal differentiation and tissue repair [16]. Poliumoside treatment similarly improved neuronal preservation and function while activating PI3K/AKT/mTOR and dampening oxidative stress, indicating a coordinated

pro-survival and pro-regenerative role [17]. Selenium nanoparticles provided another route to neuroprotection: by regulating PI3K-AKT-mTOR alongside Ras-MEK signaling, they reduced oxidative cytotoxicity and spinal neuron apoptosis while avoiding immunosuppression [18]. However, the relationship between PI3K/AKT/mTOR and survival is not strictly unidirectional, because autophagy—often neuroprotective after SCI—can be inhibited by excessive mTOR activity. Several studies show benefit from partial pathway suppression to restore autophagic flux and thereby reduce apoptosis. BMMSCs regulated miR-202-3p to restrain mTOR activation, enhance autophagy, and suppress neuronal apoptosis [19]. In a bioinformatics-guided study, inhibition of the CCL2-PI3K/Akt axis increased protective autophagy markers and decreased apoptotic proteins, improving injury outcomes [20]. These data highlight a stage- and context-dependent model: early or moderate PI3K/AKT/mTOR activation can support survival directly, whereas controlled suppression may be beneficial when autophagy is impaired.

5.3 Regulating Inflammatory Response and Immune Microenvironment

Post-SCI inflammation is a double-edged process, with early M1-like microglia/macrophage activation amplifying tissue damage and later M2-like polarization supporting repair. PI3K/AKT/mTOR signaling contributes to immune phenotype control and cytokine output, but again in a highly cell-specific fashion. Several biomaterial and exosome-based approaches promote an anti-inflammatory milieu through PI3K/AKT/mTOR-linked M2 polarization. A Lycium barbarum oligosaccharide-primed MSC hydrogel enhanced M2 microglial polarization by activating PI3K-Akt-mTOR, improving the microenvironment for repair [21]. Conversely, multiple pain- and inflammation-focused studies report that suppressing PI3K/AKT/mTOR in activated microglia boosts autophagy and dampens inflammatory injury. Peripheral macrophage-derived exosomes inhibited PI3K/AKT/mTOR to increase microglial autophagy and promote anti-inflammatory polarization [22]. MSC-EV-transferred miR-99b-3p reduced microglial activation and neuropathic pain via PI3K/AKT/mTOR inhibition and autophagy restoration [23]. Minocycline likewise alleviated SCI-related neuropathic pain through suppression of PI3K/AKT/mTOR and induction of autophagy [24]. These findings suggest that therapeutic calibration rather than uniform activation is crucial: promoting PI3K/AKT/mTOR activity may favor M2 reparative states in some immune populations, whereas transient inhibition in over-activated microglia can restore autophagic homeostasis and reduce pro-inflammatory toxicity.

5.4 Promoting Angiogenesis and Improving Microcirculation

Vascular disruption and ischemia are major drivers of secondary degeneration, and revascularization is necessary to sustain neural repair. PI3K/AKT/mTOR signaling is a canonical mediator of endothelial survival, migration, and tube formation, acting downstream of growth factors such as BDNF and VEGF. A neural-enhancing PRP/Alg/GelMA triple-network hydrogel incorporating BDNF promoted both neurogenesis and vascular regeneration after SCI; mechanistically, its pro-angiogenic effects were attributed to PI3K/AKT/mTOR activation in endothelial and neural stem cell compartments [25]. Exosomes and biomaterials that modulate the inflammatory vasculo-immune interface further enhance microcirculatory recovery. For example, UTX-regulated endothelial exosomes shaped macrophage phenotypes via PI3K/AKT/mTOR, indirectly improving the vascular microenvironment that supports regeneration [26]. Improved perfusion also feeds forward into reduced oxidative stress and apoptosis, creating a vascular-neural coupling in which PI3K/AKT/mTOR serves as a shared molecular hub. Thus, angiogenic strategies engaging this pathway may provide additive benefit by simultaneously supporting endothelial recovery and neuronal resilience.

5.5 Promoting Neural Stem Cell Differentiation and Neurogenesis

Endogenous and transplanted neural stem cells (NSCs) contribute to circuit reconstruction by differentiating into neurons and oligodendrocytes while limiting astroglial scarring. PI3K/AKT/mTOR signaling is central to NSC fate decisions, promoting neuronal and oligodendrocyte differentiation in many contexts. Magnetic nanoparticle-assisted NSC transplantation activated PI3K/AKT/mTOR and biased NSCs toward neuronal lineages, improving axonal regeneration and functional outcomes [27]. Electroconductive hydrogels combined with BMSC-exosomes enhanced NSC recruitment and promoted neuronal/oligodendrocyte differentiation while inhibiting astrocytic differentiation; these effects co-occurred with increased axon outgrowth via PTEN/PI3K/AKT/mTOR signaling [28]. A bioactive peptide hydrogel scaffold also stimulated NSC proliferation and neuronal differentiation in vitro and in vivo, with pathway activation proposed as a key mechanism [29]. PI3K/AKT/mTOR-linked neurogenesis is also intertwined with autophagy control. These biological factors enhanced NSC neuronal differentiation and improved motor recovery by activating PI3K/AKT/mTOR and restraining excessive autophagy after traumatic SCI. Together, these studies suggest that PI3K/AKT/mTOR provides a permissive intracellular state for NSCs to generate neurons and oligodendroglia needed for network repair, while careful regulation of downstream autophagy is required to avoid maladaptive outcomes.

6. Conclusion and Perspective

The PI3K/AKT/mTOR signaling pathway plays a central and highly versatile role in the complex pathophysiology of spinal cord injury. As demonstrated across current research, this pathway integrates extracellular growth cues, metabolic state, and cellular stress signals to regulate neuronal survival, axonal regeneration, autophagy, inflammation, angiogenesis, and stem cell behavior [30]. Because SCI involves simultaneous disruption of multiple cellular and molecular systems, the broad regulatory reach of PI3K/AKT/mTOR makes it an especially promising target for multi-mechanistic therapeutic strategies.

Cumulative evidence indicates that enhancing PI3K/AKT/mTOR activity in neurons and oligodendrocyte

lineage cells can significantly improve axon regrowth, synaptic plasticity, and remyelination [31]. Equally important is the pathway's anti-apoptotic and neuroprotective influence, which helps preserve residual neural networks during the critical early post-injury period. Regulation of the inflammatory microenvironment has emerged as another major therapeutic avenue; appropriately timed modulation of PI3K/AKT/mTOR can shift microglia/macrophages toward reparative phenotypes, reduce cytokine-mediated secondary injury, and improve overall tissue integrity [32]. Additionally, targeted activation of the pathway in endothelial cells stimulates angiogenesis and vascular stabilization, thereby restoring microcirculation and nutrient delivery. Its influence on neural stem/progenitor cells further highlights its potential in promoting endogenous neurogenesis and enhancing the survival and differentiation of transplanted cells [33].

Despite this progress, several challenges remain before translation to clinical therapies. First, the pathway's effects are highly cell-type and context dependent; global activation may produce adverse outcomes such as excessive glial scar formation, suppressed autophagy, or oncogenic risks [34]. Thus, future work must prioritize precise spatial, temporal, and cell-specific modulation—potentially via nanoparticle systems, engineered extracellular vesicles, small-molecule isoform-selective activators/inhibitors, or gene-editing tools. Second, the interplay between PI3K/AKT/mTOR and other pathways (MAPK, JAK/STAT, Wnt/β-catenin, RhoA/ROCK) suggests that combinatorial interventions may outperform single-target therapies. Third, large-animal research and standardized outcome measures are needed to facilitate clinical translation.

Looking forward, an integrated therapeutic paradigm — combining PI3K/AKT/mTOR modulation with biomaterials, stem-cell transplantation, neurorehabilitation, and multi-pathway targeting—is likely to yield the most robust improvement in neural repair. Continued advances in molecular delivery systems, high-resolution cell-type mapping, and systems biology will accelerate the development of safe and effective treatments. Harnessing the full therapeutic potential of the PI3K/AKT/mTOR pathway may ultimately provide a powerful strategy to overcome the barriers to regeneration and restore meaningful function after spinal cord injury.

References

[1] Lo J, Chan L, Flynn S. A Systematic Review of the Incidence, Prevalence, Costs, and Activity and Work Limitations of Amputation, Osteoarthritis, Rheumatoid Arthritis, Back Pain, Multiple Sclerosis, Spinal Cord Injury, Stroke, and Traumatic Brain Injury in the United States: A 2019 Update. Arch Phys Med Rehabil. 2021; 102(1): 115-131.

[2] Hu X, Xu W, Ren Y, et al. Spinal cord injury: molecular mechanisms and therapeutic interventions. Signal Transduct Target Ther. 2023;8(1):245.

[3] Hellenbrand DJ, Quinn CM, Piper ZJ, Morehouse CN, Fixel JA, Hanna AS. Inflammation after spinal cord injury: a review of the critical timeline of signaling cues and cellular infiltration. J Neuroinflammation. 2021; 18(1): 284. Published 2021 Dec 7.

[4] Tian T, Zhang S, Yang M. Recent progress and challenges in the treatment of spinal cord injury. Protein Cell. 2023; 14(9): 635-652.

[5] Li R, Zheng Y, Zhang J, Zhou Y, Fan X. Gomisin N attenuated cerebral ischemia-reperfusion injury through inhibition of autophagy by activating the PI3K/AKT/mTOR pathway. Phytomedicine. 2023; 110: 154644.

[6] Ruiz de Almodovar C, Dupraz S, Bonanomi D. Neurovascular dynamics in the spinal cord from development to pathophysiology. Neuron. 2025; 113(24): 4134-4157.

[7] Yu M, Wang Z, Wang D, Aierxi M, Ma Z, Wang Y. Oxidative stress following spinal cord injury: From molecular mechanisms to therapeutic targets. J Neurosci Res. 2023;101(10):1538-1554.

[8] Jiang M, Zhang K, Zhang Z, et al. PI3K/AKT/mTOR Axis in Cancer: From Pathogenesis to Treatment. MedComm (2020). 2025;6(8):e70295. Published 2025 Jul 30.

[9] Yu L, Wei J, Liu P. Attacking the PI3K/Akt/mTOR signaling pathway for targeted therapeutic treatment in human cancer. Semin Cancer Biol. 2022; 85: 69-94.

[10] Tang Q, Markby GR, MacNair AJ, et al. TGF-β-induced PI3K/AKT/mTOR pathway controls myofibroblast differentiation and secretory phenotype of valvular interstitial cells through the modulation of cellular senescence in a naturally occurring in vitro canine model of myxomatous mitral valve disease. Cell Prolif. 2023; 56(6): e13435.

[11] Karova K, Polcanova Z, Knight L, et al. Hyperactive delta isoform of PI3 kinase enables long-distance regeneration of adult rat corticospinal tract. Mol Ther. 2025; 33(2):752-770.

[12] Campion TJ 3rd, Sheikh IS, Smit RD, et al. Viral expression of constitutively active AKT3 induces CST axonal sprouting and regeneration, but also promotes seizures. Exp Neurol. 2022; 349: 113961.

[13] Shu H, Zhang X, Pu Y, et al. Fucoidan improving spinal cord injury recovery: Modulating microenvironment and promoting remyelination. CNS Neurosci Ther. 2024; 30(8): e14903.

[14] Ding Z, Dai C, Zhong L, et al. Neuregulin-1 converts reactive astrocytes toward oligodendrocyte lineage cells via upregulating the PI3K-AKT-mTOR pathway to repair spinal cord injury. Biomed Pharmacother. 2021; 134:111168.

[15] Sun X, Huang LY, Pan HX, et al. Bone marrow mesenchymal stem cells and exercise restore motor function following spinal cord injury by activating PI3K/AKT/mTOR pathway. Neural Regen Res. 2023; 18(5): 1067-1075.

[16] Zhang W, Liu M, Ren J, et al. Magnetic Nanoparticles and Methylprednisolone Based Physico-Chemical Bifunctional Neural Stem Cells Delivery System for Spinal Cord Injury Repair. Adv Sci (Weinh). 2024; 11(21): e2308993.

[17] Li Q, Hong H, Xu G, et al. Poliumoside Alleviates Neuroinflammation and Oxidative Stress After Spinal Cord Injury by Activating the PI3K/AKT/mTOR Signaling Pathway. J Integr Neurosci. 2025; 24(10): 43900.

[18] Liu P, Liu X, Wu Z, et al. Size effect-based improved antioxidant activity of selenium nanoparticles regulating Anti-PI3K-mTOR and Ras-MEK pathways for treating spinal cord injury to avoid hormone shock-induced immunosuppression. J Nanobiotechnology. 2025; 23(1): 17.
[19] Huang K, Fang J, Sun W, et al. Bone marrow mesenchymal stem cells modulate miR-202-3p to suppress neuronal apoptosis following spinal cord injury through autophagy activation via the AMPK, MAPK, and PI3K/AKT/mTOR signaling pathway. Sci Rep. 2024;14(1):30099.
[20] Fang S, Tang H, Li MZ, Chu JJ, Yin ZS, Jia QY. Identification of the CCL2 PI3K/Akt axis involved in autophagy and apoptosis after spinal cord injury. Metab Brain Dis. 2023;38(4):1335-1349.
[21] Yu Q, Liao M, Sun C, et al. LBO-EMSC Hydrogel Serves a Dual Function in Spinal Cord Injury Restoration via the PI3K-Akt-mTOR Pathway. ACS Appl Mater Interfaces. 2021;13(41):48365-48377.
[22] Zhang B, Lin F, Dong J, Liu J, Ding Z, Xu J. Peripheral Macrophage-derived Exosomes promote repair after Spinal Cord Injury by inducing Local Anti-inflammatory type Microglial Polarization via Increasing Autophagy. Int J Biol Sci. 2021; 17(5): 1339-1352.
[23] Gao X, Gao LF, Kong XQ, Zhang YN, Jia S, Meng CY. Mesenchymal stem cell-derived extracellular vesicles carrying miR-99b-3p restrain microglial activation and neuropathic pain by stimulating autophagy. Int Immunopharmacol. 2023; 115: 109695.
[24] Qiao L, Tang Q, An Z, Qi J. Minocycline relieves neuropathic pain in rats with spinal cord injury via activation of autophagy and suppression of PI3K/Akt/mTOR pathway. J Pharmacol Sci. 2023; 153(1): 12-21.
[25] Yun Z, Wu J, Sun X, et al. Neural-enhancing PRP/Alg/GelMA triple-network hydrogel for neurogenesis and angiogenesis after spinal cord injury via PI3K/AKT/mTOR signaling pathway. Theranostics. 2025; 15(9):3837-3861.
[26] Peng W, Xie Y, Luo Z, et al. UTX deletion promotes M2 macrophage polarization by epigenetically regulating endothelial cell-macrophage crosstalk after spinal cord injury. J Nanobiotechnology. 2023; 21(1): 225.
[27] Zhang W, Liu M, Ren J, et al. Magnetic Nanoparticles and Methylprednisolone Based Physico-Chemical Bifunctional Neural Stem Cells Delivery System for Spinal Cord Injury Repair. Adv Sci (Weinh). 2024; 11(21): e2308993.
[28] Fan L, Liu C, Chen X, et al. Exosomes-Loaded Electroconductive Hydrogel Synergistically Promotes Tissue Repair after Spinal Cord Injury via Immunoregulation and Enhancement of Myelinated Axon Growth. Adv Sci (Weinh). 2022;9(13):e2105586.
[29] Sun Z, Luan X, Sun Z, et al. Bioactive Peptide Hydrogel Scaffold with High Fluidity, Thermosensitivity, and Neurotropism in 3D Spatial Structure for Promoted Repair of Spinal Cord Injury. Small. 2025; 21(2): e2406990.
[30] Chen CH, Sung CS, Huang SY, et al. The role of the PI3K/Akt/mTOR pathway in glial scar formation following spinal cord injury. Exp Neurol. 2016; 278: 27-41.
[31] Wang Z, Zhou L, Zheng X, et al. Autophagy protects against PI3K/Akt/mTOR-mediated apoptosis of spinal cord neurons after mechanical injury. Neurosci Lett. 2017; 656: 158-164.
[32] Abbaszadeh F, Fakhri S, Khan H. Targeting apoptosis and autophagy following spinal cord injury: Therapeutic approaches to polyphenols and candidate phytochemicals. Pharmacol Res. 2020; 160: 105069.
[33] Chen G, Li J, Wang Z, Liu W. Ezetimibe protects against spinal cord injury by regulating autophagy and apoptosis through inactivation of PI3K/AKT/mTOR signaling. Am J Transl Res. 2020;12(6):2685-2694.
[34] Wang Z, Zheng S, Gu Y, Zhou L, Lin B, Liu W. 4-PBA Enhances Autophagy by Inhibiting Endoplasmic Reticulum Stress in Recombinant Human Beta Nerve Growth Factor-Induced PC12 cells After Mechanical Injury via PI3K/AKT/mTOR Signaling Pathway. World Neurosurg. 2020;138:e659-e664.