REVIEW ARTICLE

Exosomes: An emerging therapeutic target for sports repair

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Sports injuries, inevitably occurring as a result of physical activity, are currently primarily addressed through methods involving pain and inflammation relief *via* medication, as well as transplant-related therapies for the repair of damaged tissues and organs subsequent to injury. However, the efficacy of these approaches in restoring functionality after injury remains less than optimal. It has been discovered that the genetic materials carried by exosomes can significantly repair damaged tissues and organs, yielding more promising functional recovery outcomes. This study provided a comprehensive review of the regenerative functions of exosomes in repairing injuries to human bones and skeletal muscles, neurological damage, cardiac injuries, pulmonary injuries, renal injuries, and skin injuries with the aim of anticipating the potential therapeutic effects and underlying mechanisms of exosomes in sports repair, offering enhanced theoretical support for the repair of sports-related injuries. The application of exosomes is very complex. The optimal source of exosomes for use in damaged sites, the specific mechanisms of miRNA action, signaling pathways, how exercise promotes exosome secretion, methods to enhance the application of exosomes in damaged tissues besides injection, and clinical trial strategies are all worthy of in-depth research.

Keywords: exosomes; sports injury; injury repair; therapy.

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Introduction

Exosomes are nano-sized vesicles, typically 30 – 100 nm in diameter, characterized by a lipid bilayer structure. They are secreted by various types of cells and carry a diverse cargo including mRNAs, microRNAs (miRNAs), lipids, and macromolecular proteins. Due to their natural protective and transport capabilities, exosomes are ideal carriers for delivering biomolecules to specific target cells. Among the genetic material carried by exosomes, miRNAs are particularly important. Emerging as a novel therapeutic approach, exosomes are gradually being utilized in clinical experiments for treating various diseases such as tumors and cancers, albeit with limited involvement in the field of sports. Empirical evidence confirms the significant effects of exosomal genetic materials derived from mesenchymal stem cells (MSCs) in the process of sports repair [1]. Exosomes demonstrate the ability to mitigate cellular apoptosis, enhance cell proliferation, promote tissue regeneration, and accomplish injury repair through intercellular substance information transfer [2]. Current research predominantly focuses on the reparative aspects of exosomes in injuries with comparatively limited exploration of exosome applications in the realm of sports, especially in the context of sports repair.

Therefore, in-depth research into the impact of exosomes on sports injury repair is crucial. This research aimed to explore exosomes as an alternative to cell therapy, paving the way for the development of new treatment strategies and innovative therapies. By providing a solid theoretical foundation for the treatment of sports injuries, this research played a crucial role in further reducing the damage caused by physical activity, thereby promoting individual health.

Exosomes

Origins of exosomes

Exosomes are cell vesicles with a density ranging from 1.13 to 1.19 g/mL and a diameter of 30 - 100 nm. They are formed through a series of processes such as endocytosis within cells, fusion with the cell membrane, and release into the extracellular environment [3, 4]. These structures are not only present in the plasma but also in various types of bodily fluids including tears, milk [5], saliva [6], semen, and urine [7]. Scientists discovered small vesicles in reticulocytes of rats [8], and these vesicles were observed during the development of reticulocytes in sheep under an electron microscope [9]. However, it was not until 1987 that these vesicles were officially termed “exosomes” [8]. Initially considered cellular debris that needed to be removed, exosomes were viewed as unnecessary "waste". This perspective persisted until 2007 when genetic materials such as miRNAs and mRNAs were first identified in exosomes. This discovery offered a new understanding of exosomes, revealing the potential involvement of their genetic contents in intercellular information transmission and communication [10]. Subsequently, in-depth studies were conducted on the composition, origins, secretion processes, mechanisms of action, and functions of exosomes. Presently, exosomes are gradually being employed in clinical experiments for disease treatments such as tumor and cancer treatments. However, a limited amount of research exists in the international sphere regarding exosomes in the domain of sports, especially in the context of sports repair.

Formation and mechanisms of exosomes action

Exosomes, characterized by a lipid bilayer structure, exhibit varying morphologies based on their hydration status. When dehydrated, exosomes adopt a flattened appearance [9, 11], while they assume a rounded shape when hydrated [5]. The intricate process of exosome formation is commonly believed to commence with the generation of early endocytic vesicles through internalization within cells. These vesicles subsequently amalgamate with a range of substances in the intracellular fluid, evolving into multivesicular bodies. Multivesicular bodies may undergo degradation by lysosomes or fusion with the cell membrane, in the latter case, their intraluminal vesicles are released into the extracellular fluid as exosomes [12, 13]. Through systemic circulation, exosomes are transported to diverse organs and tissues, influencing various biological systems. A fraction of exosomes remains within the intracellular fluid, serving as essential mediators or vehicles for facilitating intercellular information exchange [14]. Despite exosomes featuring prominently in the exploration of numerous diseases, their precise mechanisms of action on recipient cells remain incompletely understood. In recent years, extensive research endeavors have been directed toward unravelling the therapeutic potentials of exosomes in disease contexts and elucidating their roles as biological indicators, which aims to unveil the intricacies of exosome signalling pathways and their modes of operation. Initially regarded as mere cellular “waste receptacles” shedding membrane proteins [11], deeper investigations have uncovered the profound impact of exosomes on facilitating intercellular communication and orchestrating cellular immune responses [15]. By activating recipient cells, exosomes trigger relevant signalling cascades, liberating proteins, RNA, and other molecular cargo into recipient cells through endocytic pathways, thereby integrating with and releasing contents into the cytoplasm of those recipient cells [16].

The role of exosomes in sports repair process

Against the backdrop of a burgeoning fitness culture, the population engaging in exercise training is steadily increasing. However, a lack of specialized theoretical knowledge and skills has led to a rising incidence of exercise-induced injuries. Suboptimal training loads and improper methodologies stand as primary culprits behind such injuries during exercise regimens. Unlike other pursuits, training carries inherent unpredictable elements, introducing a certain risk of exercise-induced injuries. Presently, conventional treatment methods for exercise-related injuries typically address symptoms superficially, yielding less than optimal outcomes. In recent years, numerous studies have substantiated the therapeutic efficacy of exosomes in the repair of exercise-induced injuries and revealed that exosomes play a crucial role in the repair of bone, neural, cardiac, and renal injuries primarily by activating the AKT signalling pathway to facilitate repair and regeneration. Moreover, exosomes contribute to tissue repair in the context of injuries by activating a variety of additional signalling pathways.

Exosomes and injuries to hard and soft tissues

(1) Exosomes and bone injury

Fractures are the most common form of traumatic injury with approximately 10 - 20% of fractures experiencing compromised or delayed healing [17, 18]. Mild fractures are typically treated using traditional external immobilization methods, which may yield less than optimal results for complex or severe fractures. Current clinical approaches involve treatments such as bone grafting and biomaterial replacement, but these methods come with drawbacks including limited sources and risks of infection and immune rejection post-transplantation. Hence, there is an urgent need to develop novel treatment strategies to expedite bone regeneration in the healing process of fractures. Mesenchymal stem cells (MSCs), known for their multipotency that can differentiate into bone cells, fat cells, cartilage cells, muscle cells, and neurons [19, 20], have been reported to participate in multiple stages of fracture healing. Differentiation of MSCs into osteoblasts is essential for bone repair [21]. Recent studies have emphasized the crucial role of miRNAs in MSC differentiation including bone formation [22]. Research focusing on microRNA-21 (miR-21) in the osteogenic differentiation of human umbilical cord mesenchymal stem cells (hUMSCs) has shown an upregulation trend in response to increased PI3K-AKT signalling pathway activity, which promotes the phosphorylation of GSK-3β, leading to the stabilization and accumulation of β-catenin in the cytoplasm to activate the transcription of RUNX-2, ultimately enhancing osteogenesis in hUMSCs [23]. miRNA-21 promotes the osteogenic differentiation of bone marrow MSCs [24], and local injection of miRNA-21-treated bone marrow MSCs has been shown to promote fracture healing in rats [24]. Furthermore, bone marrow mesenchymal stem cells (BMSCs) hold strong appeal for bone regeneration treatments such as osteogenic differentiation [25]. It has been demonstrated that bone marrow-derived BMSCs, as opposed to adipose-derived BMSCs, exhibit greater osteogenic differentiation potential [25]. Through a mouse femoral fracture model, comparison between wild-type mice and CD92/2 mice has shown that the former exhibit faster fracture healing than the latter, and injection of exosomes into CD92/2 mice significantly reduces healing time, accelerating bone injury repair [26]. Further studies have revealed that exosomes released from β-tricalcium phosphate (β-TCP) can be internalized by human bone marrow mesenchymal stem cells (hBMSCs), significantly promoting cell proliferation, migration, and osteogenic differentiation. Compared to a solely β-TCP scaffold, a composite scaffold of exosomes and β-TCP enhances bone formation through the activation of the PI3K-Akt signalling pathway [27]. The biologically active properties of biomaterials can be enhanced through exosomes, and hiPSC-MSC-Exos, exosomes secreted by human induced pluripotent stem cell-derived MSCs, combined with a β-TCP scaffold are effective for bone injury repair. The

β-TCP + hiPSC-MSC-EXOS scaffold combination covers most of the bone defect area, significantly promoting the expression of bone formation and angiogenesis markers in the defect area with efficacy increasing with concentration [28]. Additionally, miR-196a plays a crucial role in osteoblast differentiation and the expression of osteogenic genes, particularly in the repair of bone injuries including critical joint cartilage repair [29]. Studies have shown that the activation of YAP protein by Wnt5a and Wnt5b through the Wnt Yap/TAZ signaling pathway leads to chondrocyte proliferation and migration with miR-140-5P consequently promoting cartilage tissue regeneration [30].

(2) Exosomes and skeletal muscle injury

High-intensity and challenging training can enhance athletic performance but may also lead to a decline in skeletal muscle function. Prolonged training sessions, excessive intensity, or inadequate warm-up can result in muscle damage and fibrosis due to overexertion. While cell therapy has shown some effectiveness in repairing damaged tissues, it is not considered the most ideal treatment method. Following muscle injuries, a rapid repair response is initiated to seal damaged cell membranes, reactivate alternative pathways, and promote muscle regeneration. During the regeneration process, cells are activated, differentiated, and fused, requiring intercellular information exchange primarily mediated through lipids, fusion membrane proteins, and exosomes [31]. In recent years, researchers have highlighted the significant potential of exosomes in the process of repairing skeletal muscle injuries. Studies utilizing a mouse muscle tear model have demonstrated that exosomes secreted by human skeletal muscle myoblasts (HSKMs) can effectively enhance muscle regeneration. These exosomes contain a variety of signalling molecules including myogenic growth factors like FGF2, HGF, and PDGF, which play a crucial role in regulating the proliferation and differentiation of muscle satellite cells. *In vivo* studies have demonstrated that injecting exosomes derived from differentiated human skeletal muscle (HSKM) cells into damaged areas increases the number of muscle fibers, reduces the extent of fibrosis, and enhances the muscle fiber content at the site of skeletal muscle injury, thereby promoting skeletal muscle regeneration in a mouse model of muscle tearing [32]. Exosomes serve as biochemical cues, guiding stem cell differentiation, offering a cell-free therapeutic approach for muscle regeneration, and representing a novel regulatory factor in the process of skeletal muscle recovery. Exosomes derived from MSCs contain low concentrations of repair-related cytokines. In a rat model of skeletal muscle regeneration injury, the injection of MSC-derived exosomes has shown to expedite tissue muscle regeneration, strengthen vascular repair capabilities, and diminish muscle fibrosis. Experimental data have identified the presence of miRNAs linked to tissue regeneration in exosomes such as miR-1, miR-133, and miR-206, which promote muscle regeneration in rat models of skeletal muscle injury [33]. Furthermore, MSC-derived exosomes also hold a substantial amount of miR-494, playing a vital role in muscle cell generation and tissue repair while enhancing muscle migration activity. These exosomes stimulate muscle regeneration through miRNA, shedding light on the mechanisms involved in skeletal muscle recovery. Apart from secreting cytokines, chemotactic factors, or growth factors during MSC transplantation, exosomes are poised to emerge as a novel therapeutic tool in the realm of muscle regeneration [34].

Exosomes and neural damage

During physical activity, the human body executes a variety of technical movements under the regulation of the neuro-humoral control system. Conversely, physical exercise also impacts the nervous system and can lead to certain damages to the human body. While physical activity enhances the functionality of different organs and systems, it can also reduce the survival rate of glial cells in the nervous system, resulting in the death of numerous glial cells. Nerve damage from exercise can significantly affect human motor function and, in

severe cases, can even lead to paralysis. On the other hand, exosomes play a crucial role as essential carriers for intercellular information transmission and communication during the neural repair process. Studies have shown that exosomes derived from vascular endothelial cells (VECs) can effectively enhance cell proliferation and migration, along with the secretion of matrix metalloproteinase-1 (MMP-1), MMP-3, and nuclear factor k when stimulated by MSCs. These factors promote the growth of neural cells [35]. MSCs originating from human adipose-derived mesenchymal stem cell exosomes (hAMSCs) express specific proteins such as CD63, CD81, HSP70, and HSP90. The protective factors crucial for the nervous system primarily include insulin-like growth factor, hepatocyte growth factor, as well as exosomes secreted by hAMSCs, which offer protection against nerve injuries. This process likely involves the activation of the PI3K-Akt signalling pathway [36], suppression of GSK-3β, and augmentation of axonal growth. Furthermore, it has been observed that endothelial cell-secreted exosomes have a significant influence on the proliferation and apoptosis of SH-SY5Y nerve cells [37]. By examining the expression levels of Bcl-2, it has been further confirmed that exosomes derived from VECs can serve as a novel therapeutic approach for treating nerve injuries. Through the injection of adipose-derived mesenchymal stem cell (ADMSCs) exosomes, a notable restoration of nerve function has been observed [38]. Research indicates that MSC-derived exosomes establish communication with cortical neurons to enhance axonal growth through the transfer of biomaterials, particularly miRNAs, which provides fresh insights into the molecular mechanisms that enhance axonal remodelling in MSC cell therapy. The role of exosomes as conveyors of specific miRNAs to cortical axons aids in the regeneration of motor neurons, essential for neural plasticity and functional recovery in post-stroke scenarios [39]. Importantly, exosomes derived from MSCs facilitate axonal growth in the cortex, indicating their ability to communicate with damaged endogenous neurons to promote axonal growth further [40]. These findings represent a promising avenue for neurological treatment, suggesting exosomes as a viable alternative to cell therapy in the development of novel therapeutic strategies [41].

Exosomes and cardiac injury

Exercise necessitates the transport of oxygen, thereby increasing cardiac output. Prolonged high-intensity exercise may potentially impact cardiac muscle cells and the cardiovascular system, leading to cardiac damage and, in severe cases, exercise-induced sudden cardiac death (SCD). Among different types of exercise such as track and field, basketball, and soccer, track and field events exhibit a higher mortality rate in exercise-induced sudden cardiac death compared to other sports. Despite the regenerative capacity of heart cells including cardiomyocytes (CMC), vascular smooth muscle cells (VXMCs), and VECs) through stem cell regeneration, their ability is limited and insufficient to fully restore damaged tissues. Currently, the common approach to alleviate symptoms caused by exercise-induced damage involves the use of defibrillators or cardiac surgery. Studies indicate that high-intensity exercise can result in adverse effects such as cardiac cell death, cardiac arrest, and cardiovascular damage. Cardiac progenitor cells (CPCs) have emerged as a potential therapy for improving cardiac repair. The paracrine factors released by CPCs can stimulate cardiac repair mechanisms including promoting blood vessel formation and inhibiting cardiomyocyte apoptosis. CPC exosomes can stimulate cardiac regeneration by increasing vascular density and reducing cardiomyocyte apoptosis [42]. Due to the limited regenerative capacity of cardiac cells, stem cells have long been favored for promoting cardiac regeneration [43]. Research has demonstrated that exosomes derived from cardiac-derived stem cells (CDCs) can enhance cardiomyocyte proliferation and angiogenesis. CDC exosomes contain significant amounts of miR-146a, a protein translated from this microRNA that inhibits the rate of cellular apoptosis, promotes cardiomyocyte proliferation

and facilitates repair of cardiovascular damage [44]. By establishing an ischemia-reperfusion rat model and administering exosomes directly into the heart muscle, it was discovered that exosomes could reduce fibrotic areas, scar sizes, and promote cell proliferation and angiogenesis [45]. While intra-myocardial injection of exosomes has shown promise in animal experiments, stringent procedures are required for clinical application [46]. Exosomes are rich in miRNAs, which play a crucial role in cardiac repair and regeneration [47]. Among them, miR-21 and miR-146a have demonstrated reparative functions for damaged cardiac muscle [48]. MiR-21 reduces cardiomyocyte apoptosis by regulating programmed cell death 4 (PDCD4), FasL, and AKT pathways [48, 49], while miR-146a inhibits interleukin-1 receptor-associated kinase 1 (IRAK1) and tumor necrosis factor (TNF) receptor-associated factor 6 (TRAF6), reducing the activation of nuclear factor κB (NF-κB) [44]. miR-146a also targets c-Fos in human cardiac cells [50]. Intensive exercise can lead to cardiac ischemia and hypoxia, causing exercise-induced cardiac damage. Exosomes, through their diverse miRNA content [51], play a role in cardiac repair and regeneration processes following cardiac injury [52].

Exosomes and lung injury

Exhaustive exercise can lead to respiratory impairments, causing harm to the pulmonary organs and resulting in lung injury. Presently, medical treatments targeting exercise-induced lung injury are limited. Studies have shown that lung injury can be alleviated by transplanting MSCs to alleviate inflammatory responses, improve damage mechanisms, and enhance survival rates. Although this approach has shown some efficacy, the extent of survival remains constrained [53]. Further investigations suggest that the paracrine effects of MSCs may play a role in lung injury repair. MSCs can secrete various paracrine factors that mitigate oxidative stress, regulate immune responses, suppress damage, and promote self-repair of damaged tissues [54]. Multiple studies indicate that, in models of lung injury, MSCs can downregulate pro-inflammatory cytokines while upregulating anti-inflammatory cytokines, thereby reducing pulmonary edema and exerting a therapeutic effect on lung injury [55]. Research has revealed that the key to cell survival and the cell cycle lies in the PI3K-Akt signalling pathway [56], and exosomes can prevent pulmonary fibrosis and promote lung injury repair possibly through mediation of the PI3K-Akt signalling pathway [57]. Numerous reports confirm the presence of anti-fibrotic miRNAs. Among them, miRNA-27 is abundantly expressed, and the transfer of miRNA-27α-3P can reduce pulmonary fibrosis [58]. hAEC Exos contain a variety of miRNAs targeting the TGF-B signal, among which miR-23α can inhibit SMAD2 [59], and miR-203a can suppress SMAD3, thereby aiding in inhibiting TGF-B-mediated epithelial-mesenchymal transition and pulmonary fibrosis [60]. These studies collectively demonstrate that exosomes significantly improve pulmonary damage and enhance pulmonary function in repeated experiments.

Exosomes and renal injury

High-intensity exercise can inflict certain injuries upon the kidneys with the most common manifestations being renal failure and hematuria. Research has revealed that exosomes secreted by MSCs and endothelial progenitor cells can inhibit apoptosis, promoting the repair and regeneration of renal tubules and renal units [61]. Further evidence suggests that the healing of renal injuries is associated with the activation of EGFR and the role of exosomes [62]. EGFR plays a crucial role in cell migration and repair post-injury, participating in the renal tubule repair process following renal injury. Furthermore, exosomes derived from umbilical cord mesenchymal stem cells (UCMSCs-exo) can boost the secretion of anti-inflammatory molecule IL-10, reduce the expression of inflammatory molecules IL-1β, IL-6, TNF-α, and IL-12P40, thereby further repairing renal inflammation [63]. The miR-30b carried by exosomes can promote the generation of endothelial cell blood vessels, restoring blood flow in mice with injuries [64], suggesting that exosomes can facilitate renal injury repair

through this series of processes. By establishing a mouse model of renal injury and injecting exosomes derived from MSCs into the damaged kidneys, it was found that the mRNA contained in exosomes can activate the Akt and ERK pathways, inhibit the expression of apoptosis genes Bax and Caspase3/7, leading to significant expression of Bcl2, thereby promoting renal cell proliferation [65]. In the mouse model of renal injury, it was also discovered that exosomes secreted by MSCs could promote renal repair by preventing apoptosis, alleviating inflammation and renal apoptosis, and increasing the proliferation of renal tubular epithelial cells. Multiple injections of exosomes further improved renal function and morphology, eliminating renal fibrosis and reducing mortality [66]. Reports suggest that the transfer of insulin-like growth factor-1 receptor (IGF-1R) mRNA to renal tubular cells also contributes to the powerful protective effect of MSC exosomes on the kidneys [67]. Exosomes derived from MSCs induce the expression of anti-apoptotic genes of Bcl-XL, Bcl2, and BIRC8 in renal tubular epithelial cells, while downregulating pro-apoptotic genes of Casp1, Casp8, and LTA, imparting the necessary anti-apoptotic phenotype for tissue repair [68]. Furthermore, MSC exosomes stimulate renal cell proliferation by inducing phosphorylation and activation of extracellular signal-regulated kinase (ERK) [69]. These data validate that MSC-derived exosomes can stimulate renal repair and/or regeneration through various pathways [70]. Exosomes serve as mediators for cell communication, transmitting information to differentiated cells, thereby promoting cell proliferation, alleviating tissue and organ damage, and playing a crucial protective role.

Exosomes and skin injury

Intense physical activity can lead not only to injuries affecting the musculoskeletal and nervous systems but also to various types of skin damage. Abrasions resulting from physical exhaustion, constrained environmental conditions, or improper training methods are quite common. However, soft tissue wounds due to their longer healing times are more prone to scar formation, not only impacting the functionality of soft tissues but also affecting the psychological well-being of patients. Therefore, accelerating the healing process and reducing scar formation in soft tissue injuries has become an urgent issue that needs to be addressed. Currently, commonly used methods to accelerate wound healing and reduce scar formation include skin grafts and laser therapy [71, 72], yet these methods have adverse effects on the body [73]. There is a necessity to seek a safe, effective, and harmless method to promote scar repair. Fat tissue, widely distributed within the human body, plays a crucial role in supporting and protecting soft tissues [74]. In recent years, fat tissue has been extensively studied for its role in wound repair. Adipose-derived stem cells (ASCs) play a significant role in tissue regeneration, where exosomes derived from ASCs, upon absorption and internalization by fibroblasts, stimulate cell migration, increase collagen synthesis, and significantly accelerate wound healing when injected into the soft tissue injury area of a mouse skin incision model. Studies on the role of exosomes and the overexpression of Nrf2 in adipose-derived stem cells (ADSCs) have found that treating skin injuries with ADSC exosomes overexpressing Nrf2 gradually leads to the repair of the wound area [75]. Injecting umbilical cord blood plasma exosomes (UCB-EXOS) into mouse skin wounds accelerates epithelial cell regeneration, reduces scar formation, promotes angiogenesis, and enhances fibroblast proliferation and migration. UCB-EXOS contains a significant amount of miR21-3p, which plays a critical mediating role in the regulatory effects induced by exosomes by inhibiting phosphatase and tension homolog (PTEN) and SPRY1 [76]. Further research has shown that the intravenous injection of ASC-Exos can regulate the ratio of type III collagen to type I collagen, TGF-β3:TGF-β1 and MMP3:TIMP1, thus reducing scar formation by modulating fibroblast differentiation and promoting skin wound repair [77]. Numerous researchers have found that exosomes secreted by stem cells in skin injury models can reduce myofiber and scar formation,

accelerate wound healing, and prevent and repair damaged tissues by enhancing the HIPPO-YAP signalling pathway and Wnt4 signalling pathway. Notably, exosomes derived from human umbilical cord MSCs have shown the ability to deliver Wnt4 to stimulate skin cell migration and proliferation for wound repair [78]. Consequently, the application of exosomes may likely represent a novel approach to treating scars.

Conclusion and outlook

Research has demonstrated the remarkable reparative functionality of exosomes in cells, organs, and beyond. Currently, exosomes are primarily applied to injured parts through injection, unveiling their reparative effects across various sites. The origin and diverse nature of exosomes also warrant consideration as different sources bestow unique characteristics upon them, potentially yielding varied outcomes derived from parent cells. The application of exosomes is highly complex. Many aspects warrant in-depth exploration including identifying the optimal source of exosomes for specific sites of injury, elucidating the precise mechanisms by which miRNAs exert their effects, mapping the relevant signaling pathways, understanding how physical exercise stimulates exosome secretion, developing methods beyond direct injection to enhance the delivery of exosomes to damaged tissues, and formulating strategies for clinical trials. These research avenues will serve as significant directions for future study, aiming to apply exosomes more effectively to the repair of sports-related injuries and to develop them into a novel therapeutic modality. Such progress holds the potential not only to advance the field of sports but also to promote overall human health and well-being.

References

1. Kuçi S, Kuçi Z, Latifi-Pupovci H, Niethammer D, Handgretinger R, Schumm M, *et al*. 2009. Adult stem cells as an alternative source of multipotential (pluripotential) cells in regenerative medicine. Curr Stem Cell Res Ther. 4(2):107-117.
2. Katsuda T, Kosaka N, Takeshita F, Ochiya T. 2013. The therapeutic potential of mesenchymal stem cell-derived extracellular vesicles. Proteomics. 13(10-11):1637-1653.
3. Gilbert GE, Novakovic VA, Shi J, Rasmussen J, Pipe SW. 2015. Platelet binding sites for factor VIII in relation to fibrin and phosphatidylserine. Blood. 126(10):1237-1244.
4. Breakefield XO, Frederickson RM, Simpson RJ. 2011. Gesicles: Microvesicle “cookies” for transient information transfer between cells. Mol Ther. 19(9):1574-1576.
5. Raposo G, Stoorvogel W. 2013. Extracellular vesicles: Exosomes, microvesicles, and friends. J Cell Biol. 200(4):373-383.
6. Aqrawi LA, Galtung HK, Vestad B, Øvstebø R, Thiede B, Rusthen S, *et al*. 2017. Identification of potential saliva and tear biomarkers in primary Sjögren’s syndrome, utilizing the extraction of extracellular vesicles and proteomics analysis. Arthritis Res Ther. 19(1):14.
7. Blijdorp CJ, Burger D, Llorente A, Martens-Uzunova ES, Erdbrügger U. 2022. Extracellular vesicles as novel players in kidney disease. J Am Soc Nephrol. 33(3):467-471.
8. Minetti G, Kaestner L, Köfeler H, Perotti C, Dorn I. 2023. Terminal maturation of human reticulocytes to red blood cells by extensive remodeling and progressive liquid ordering of membrane lipids. bioRxiv. 2023:543386.
9. Pan BT, Teng K, Wu C, Adam M, Johnstone RM. 1985. Electron microscopic evidence for externalization of the transferrin receptor in vesicular form in sheep reticulocytes. J Cell Biol. 101(3):942-948.
10. Jeong JO, Han JW, Kim JM, Cho HJ, Park C, Lee N, *et al*. 2011. Malignant tumor formation after transplantation of short-term cultured bone marrow mesenchymal stem cells in experimental myocardial infarction and diabetic neuropathy. Circ Res. 108(11):1340-1347.
11. Pan BT, Johnstone RM. 1983. Fate of the transferrin receptor during maturation of sheep reticulocytes *in vitro*: Selective externalization of the receptor. Cell. 33(3):967-978.
12. Huotari J, Helenius A. 2011. Endosome maturation. EMBO J. 30(17):3481-3500.
13. Kowal J, Tkach M, Théry C. 2014. Biogenesis and secretion of exosomes. Curr Opin Cell Biol. 29:116-125.
14. Sahoo S, Losordo DW. 2014. Exosomes and cardiac repair after myocardial infarction. Circ Res. 114(2):333-344.
15. Hsieh ML, Nishizaki D, Adashek JJ, Kato S, Kurzrock R. 2025. Toll-like receptor 3: A double-edged sword. Biomark Res. 13(1):32.
16. Li C, Liu C, Ma H, Zhang Z, Zhang J. 2025. Lymphocytes-associated extracellular vesicles activate natural killer cells in HNSCC. Cancer Sci. 116(3):633-642.
17. Einhorn TA, Gerstenfeld LC. 2015. Fracture healing: Mechanisms and interventions. Nat Rev Rheumatol. 11(1):45-54.
18. Wagner TM, Torres-Puig S, Yimthin T, Irobalieva RN, Heller M, Kaessmeyer S, *et al*. 2025. Extracellular vesicles of minimalistic Mollicutes as mediators of immune modulation and horizontal gene transfer. Commun Biol. 8(1):674.

19. Pittenger MF, Mackay AM, Beck SC, Jaiswal RK, Douglas R, Mosca JD, *et al*. 1999. Multilineage potential of adult human mesenchymal stem cells. Science. 284(5411):143-147.
20. Aprile D, Patrone D, Peluso G, Galderisi U. 2024. Multipotent/pluripotent stem cell populations in stromal tissues and peripheral blood: Exploring diversity, potential, and therapeutic applications. Stem Cell Res Ther. 15(1):139.
21. Malyaran H, Craveiro RB, Mert S, Niederau C, Maas SL, van der Vorst EPC, *et al*. 2024. Identifying differences in molecular characteristics relevant for remodeling of periodontal ligament stem cells from the upper and lower jaw. Int J Mol Sci. 25(6):3207.
22. Li H, Yang F, Wang Z, Fu Q, Liang A. 2015. microRNA-21 promotes osteogenic differentiation by targeting small mothers against decapentaplegic 7. Mol Med Rep. 12(1):1561-1567.
23. Meng YB, Li X, Li ZY, Zhao J, Yuan XB, Ren Y, *et al*. 2015. microRNA-21 promotes osteogenic differentiation of mesenchymal stem cells by the PI3K/β-catenin pathway. J Orthop Res. 33(7):957-964.
24. Sun Y, Xu L, Huang S, Hou Y, Liu Y, Chan KM, *et al*. 2015. miR-21 overexpressing mesenchymal stem cells accelerate fracture healing in a rat closed femur fracture model. Biomed Res Int. 2015:412327.
25. Lotfy A, Salama M, Zahran F, Jones E, Badawy A, Sobh M. 2014. Characterization of mesenchymal stem cells derived from rat bone marrow and adipose tissue: A comparative study. Int J Stem Cells. 7(2):135-142.
26. Furuta T, Miyaki S, Ishitobi H, Ogura T, Kato Y, Kamei N, *et al*. 2016. Mesenchymal stem cell-derived exosomes promote fracture healing in a mouse model. Stem Cells Transl Med. 5(12):1620-1630.
27. Zhang J, Liu X, Li H, Chen C, Hu B, Niu X, *et al*. 2016. Exosomes/tricalcium phosphate combination scaffolds can enhance bone regeneration by activating the PI3K/Akt signaling pathway. Stem Cell Res Ther. 7(1):136.
28. Qi X, Zhang J, Yuan H, Xu Z, Li Q, Niu X, *et al*. 2016. Exosomes secreted by human-induced pluripotent stem cell-derived mesenchymal stem cells repair critical-sized bone defects through enhanced angiogenesis and osteogenesis in osteoporotic rats. Int J Biol Sci. 12(7):836-849.
29. Qin Y, Wang L, Gao Z, Chen G, Zhang C. 2016. Bone marrow stromal/stem cell-derived extracellular vesicles regulate osteoblast activity and differentiation *in vitro* and promote bone regeneration *in vivo*. Sci Rep. 6(1):21961.
30. Tao SC, Yuan T, Zhang YL, Yin WJ, Guo SC, Zhang CQ. 2017. Exosomes derived from miR-140-5p-overexpressing human synovial mesenchymal stem cells enhance cartilage tissue regeneration and prevent osteoarthritis of the knee in a rat model. Theranostics. 7(1):180-195.
31. Demonbreun AR, McNally EM. 2017. Muscle cell communication in development and repair. Curr Opin Pharmacol. 34:7-14.
32. Han S, Fang J, Yu L, Li B, Hu Y, Chen R, *et al*. 2023. Serum-derived exosomal hsa-let-7b-5p as a biomarker for predicting the severity of coronary stenosis in patients with coronary heart disease and hyperglycemia. Mol Med Rep. 28(5):203.
33. Zhang X, Zhong Y, Rajabi S. 2025. Polyphenols and post-exercise muscle damage: A comprehensive review of literature. Eur J Med Res. 30(1):260.
34. Nakamura Y, Miyaki S, Ishitobi H, Matsuyama S, Nakasa T, Kamei N, *et al*. 2015. Mesenchymal-stem-cell-derived exosomes accelerate skeletal muscle regeneration. FEBS Lett. 589(11):1257-1265.
35. Hofer HR, Tuan RS. 2016. Secreted trophic factors of mesenchymal stem cells support neurovascular and musculoskeletal therapies. Stem Cell Res Ther. 7(1):131.
36. Xiao B, Chai Y, Lv S, Ye M, Wu M, Xie L, *et al*. 2017. Endothelial cell-derived exosomes protect SH-SY5Y nerve cells against ischemia/reperfusion injury. Int J Mol Med. 40(4):1201-1209.
37. Wei JJ, Chen YF, Xue CL, Ma BT, Shen YM, Guan J, *et al*. 2016. Protection of nerve injury with exosome extracted from mesenchymal stem cell. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 38(1):33-36.
38. Chen KH, Chen CH, Wallace CG, Yuen CM, Kao GS, Chen YL, *et al*. 2016. Intravenous administration of xenogenic adipose-derived mesenchymal stem cells (ADMSC) and ADMSC-derived exosomes markedly reduced brain infarct volume and preserved neurological function in rat after acute ischemic stroke. Oncotarget. 7(46):74537-74556.
39. Xin H, Li Y, Liu Z, Wang X, Shang X, Cui Y, *et al*. 2013. MiR-133b promotes neural plasticity and functional recovery after treatment of stroke with multipotent mesenchymal stromal cells in rats via transfer of exosome-enriched extracellular particles. Stem Cells. 31(12):2737-2746.
40. Zhang Y, Chopp M, Liu XS, Katakowski M, Wang X, Tian X, *et al*. 2017. Exosomes derived from mesenchymal stromal cells promote axonal growth of cortical neurons. Mol Neurobiol. 54(4):2659-2673.
41. Wong N, Muthiah K. 2023. Vericiguat: A new weapon in the heart failure arsenal. Medicine Today. 24(7):43-45.
42. Mol EA, Goumans MJ, Sluijter JPG. 2017. Cardiac progenitor-cell derived exosomes as cell-free therapeutic for cardiac repair. Adv Exp Med Biol. 998:207-219.
43. Bergmann O, Bhardwaj RD, Bernard S, Zdunek S, Barnabé-Heider F, Walsh S, *et al*. 2009. Evidence for cardiomyocyte renewal in humans. Science. 324(5923):98-102.
44. Ibrahim AG, Cheng K, Marbán E. 2014. Exosomes as critical agents of cardiac regeneration triggered by cell therapy. Stem Cell Reports. 2(5):606-619.
45. Vandergriff A, Huang K, Shen D, Hu S, Hensley MT, Caranasos TG, *et al*. 2018. Targeting regenerative exosomes to myocardial infarction using cardiac homing peptide. Theranostics. 8(7):1869-1878.
46. Cadmus S, Akinseye VO, van Soolingen D. 2019. Mycobacterium bovis in humans and m. tuberculosis in animals in Nigeria: An overview from 1975-2014. Int J Tuberc Lung Dis. 23(11):1162-1170.
47. Vyas N, Dhawan J. 2017. Exosomes: Mobile platforms for targeted and synergistic signaling across cell boundaries. Cell Mol Life Sci. 74(9):1567-1576.
48. Huang W, Tian SS, Hang PZ, Sun C, Guo J, Du ZM. 2016. Combination of microRNA-21 and microRNA-146a attenuates

cardiac dysfunction and apoptosis during acute myocardial infarction in mice. Mol Ther Nucleic Acids. 5:e296.
49. Wang J, Liew OW, Richards AM, Chen YT. 2016. Overview of microRNAs in cardiac hypertrophy, fibrosis, and apoptosis. Int J Mol Sci. 17(5):E749.
50. Palomer X, Capdevila-Busquets E, Botteri G, Davidson MM, Rodríguez C, Martínez-González J, *et al*. 2015. miR-146a targets Fos expression in human cardiac cells. Dis Model Mech. 8(9):1081-1091.
51. Safari S, Malekvandfard F, Babashah S, Alizadehasl A, Sadeghizadeh M, Motavaf M. 2016. Mesenchymal stem cell-derived exosomes: A novel potential therapeutic avenue for cardiac regeneration. Cell Mol Biol (Noisy-le-grand). 62(7):66-73.
52. Teng X, Chen L, Chen W, Yang J, Yang Z, Shen Z. 2015. Mesenchymal stem cell-derived exosomes improve the microenvironment of infarcted myocardium contributing to angiogenesis and anti-inflammation. Cell Physiol Biochem. 37(6):2415-2424.
53. Moodley Y, Sturm M, Shaw K, Shimbori C, Tan DB, Kolb M, *et al*. 2016. Human mesenchymal stem cells attenuate early damage in a ventilated pig model of acute lung injury. Stem Cell Res. 17(1):25-31.
54. Feng Y, Lu J, Jiang J, Shen K, Guo K, Zhong Y, *et al*. 2025. Mesenchymal stem cells for lung diseases: Focus on immunomodulatory action. Cell Death Discov. 11(1):52.
55. Asami T, Ishii M, Namkoong H, Yagi K, Tasaka S, Asakura T, *et al*. 2018. Anti-inflammatory roles of mesenchymal stromal cells during acute *Streptococcus pneumoniae* pulmonary infection in mice. Cytotherapy. 20(3):302-313.
56. Tan JL, Lau SN, Leaw B, Nguyen HPT, Salamonsen LA, Saad MI, *et al*. 2018. Amnion epithelial cell-derived exosomes restrict lung injury and enhance endogenous lung repair. Stem Cells Transl Med. 7(2):180-196.
57. Vergadi E, Ieronymaki E, Lyroni K, Vaporidi K, Tsatsanis C. 2017. Akt signaling pathway in macrophage activation and M1/M2 polarization. J Immunol. 198(3):1006-1014.
58. Cui H, Banerjee S, Xie N, Ge J, Liu RM, Matalon S, *et al*. 2016. MicroRNA-27a-3p is a negative regulator of lung fibrosis by targeting myofibroblast differentiation. Am J Respir Cell Mol Biol. 54(6):843-852.
59. Zhu T, Gao P, Gao J, Liu X, Zhang X. 2021. A huge recurrent retroperitoneal inflammatory myofibroblastic tumor implicating renal and ureter: a case report. Transl Cancer Res. 10(10):4565-4570.
60. Reddy M, Fonseca L, Gowda S, Chougule B, Hari A, Totey S. 2016. Human adipose-derived mesenchymal stem cells attenuate early stage of bleomycin induced pulmonary fibrosis: Comparison with pirfenidone. Int J Stem Cells. 9(2):192-206.
61. Ståhl AL, Johansson K, Mossberg M, Kahn R, Karpman D. 2019. Exosomes and microvesicles in normal physiology, pathophysiology, and renal diseases. Pediatr Nephrol. 34(1):11-30.
62. Blethen K, Sprowls S, Arsiwala T, Fladeland R, Panchal D, Shah N, *et al*. 2021. SYST-02. Dual inhibition of BCL-2 and EGFR in a preclinical model of lung cancer brain metastasis. Neurooncol Adv. 3(Suppl 4):iv8.
63. Bai X, Chen T, Li Y, Ge X, Qiu C, Gou H, *et al*. 2023. PD-L1 expression levels in mesenchymal stromal cells predict their therapeutic values for autoimmune hepatitis. Stem Cell Res Ther. 14(1):370.
64. Gong M, Yu B, Wang J, Wang Y, Liu M, Paul C, *et al*. 2017. Mesenchymal stem cells release exosomes that transfer miRNAs to endothelial cells and promote angiogenesis. Oncotarget. 8(28):45200-45212.
65. Lin KC, Yip HK, Shao PL, Wu SC, Chen KH, Chen YT, *et al*. 2016. Combination of adipose-derived mesenchymal stem cells (ADMSC) and ADMSC-derived exosomes for protecting kidney from acute ischemia-reperfusion injury. Int J Cardiol. 216:173-185.
66. Monsel A, Zhu YG, Gudapati V, Lim H, Lee JW. 2016. Mesenchymal stem cell derived secretome and extracellular vesicles for acute lung injury and other inflammatory lung diseases. Expert Opin Biol Ther. 16(7):859-871.
67. Tomasoni S, Longaretti L, Rota C, Morigi M, Conti S, Gotti E, *et al*. 2013. Transfer of growth factor receptor mRNA *via* exosomes unravels the regenerative effect of mesenchymal stem cells. Stem Cells Dev. 22(5):772-780.
68. Bruno S, Grange C, Collino F, Deregibus MC, Cantaluppi V, Biancone L, *et al*. 2012. Microvesicles derived from mesenchymal stem cells enhance survival in a lethal model of acute kidney injury. PLoS One. 7(3):e33115.
69. Zhou Y, Xu H, Xu W, Wang B, Wu H, Tao Y, *et al*. 2013. Exosomes released by human umbilical cord mesenchymal stem cells protect against cisplatin-induced renal oxidative stress and apoptosis in vivo and in vitro. Stem Cell Res Ther. 4(2):34.
70. Krause M, Samoylenko A, Vainio SJ. 2015. Exosomes as renal inductive signals in health and disease, and their application as diagnostic markers and therapeutic agents. Front Cell Dev Biol. 3:65.
71. Hu ZC, Chen D, Guo D, Liang YY, Zhang J, Zhu JY, *et al*. 2015. Randomized clinical trial of autologous skin cell suspension combined with skin grafting for chronic wounds. Br J Surg. 102(2):e117-e123.
72. Loreti EH, Pascoal VL, Nogueira BV, Silva IV, Pedrosa DF. 2015. Use of laser therapy in the healing process: A literature review. Photomed Laser Surg. 33(2):104-116.
73. Hu L, Wang J, Zhou X, Xiong Z, Zhao J, Yu R, *et al*. 2016. Exosomes derived from human adipose mesenchymal stem cells accelerates cutaneous wound healing *via* optimizing the characteristics of fibroblasts. Sci Rep. 6(1):32993.
74. Grainger DW. 2015. Fat prospects for healing cutaneous wounds: new activities under the sheets. Diabetes. 64(8):2717-2719.
75. Polaka S, Pawar B, Vasdev N, Tekade RK. 2024. Development and biological evaluation of smart powder bandage for wound healing and dressing applications. Int J Biol Macromol. 258(Pt 2):129044.
76. Hu Y, Rao SS, Wang ZX, Cao J, Tan YJ, Luo J, *et al*. 2018. Exosomes from human umbilical cord blood accelerate cutaneous wound healing through miR-21-3p-mediated promotion of angiogenesis and fibroblast function. Theranostics. 8(1):169-184.

77. Wang L, Hu L, Zhou X, Xiong Z, Zhang C, Shehada HMA, *et al*. 2017. Exosomes secreted by human adipose mesenchymal stem cells promote scarless cutaneous repair by regulating extracellular matrix remodelling. Sci Rep. 7(1):13321.
78. Zhang B, Wu X, Zhang X, Sun Y, Yan Y, Shi H, *et al*. 2015. Human umbilical cord mesenchymal stem cell exosomes enhance angiogenesis through the Wnt4/β-catenin pathway. Stem Cells Transl Med. 4(5):513-522.