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Review

The role of mesenchymal stem cell exosomes in cancer biology

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ABSTRACT

Mesenchymal stem cells (MSCs) have sparked considerable interest in cancer research due to their ability to influence various stages of tumor development, from initiation to metastasis. A particularly intriguing aspect of MSC behavior is their communication with cancer cells via exosome-mediated signaling. These small, extracellular vesicles released by MSCs carry a rich cargo of proteins, lipids, and nucleic acids that can drastically alter the behavior of nearby and even distant cancer cells. This review explores the multifaceted role of MSC-derived exosomes in cancer biology. It examines their formation, molecular components, and modes of communication with cancer cells. We discuss their regulatory impact on tumor behavior, ranging from angiogenesis and migration to invasion, apoptosis, and cell proliferation, emphasizing the molecular pathways that mediate these interactions. In addition, we consider their therapeutic promise, especially their potential to serve as immunomodulatory agents and targeted drug delivery platforms in oncology.

Keywords: Cancer, exosome, mesenchymal stem cells, therapy.

Mesenchymal stem cells (MSCs) are multipotent stromal cells known for their robust growth, ability to home to injury sites, and low immunogenicity in laboratory settings. Their capacity to differentiate into a variety of cell types-including chondrocytes, adipocytes, and osteoblasts-makes them essential for tissue repair and regeneration.[1] Their immunomodulatory abilities further enhance their therapeutic value, as they can modulate immune responses and support vascular development.[2] For instance, studies on umbilical cord (UC)-derived MSCs suggest they enhance bone formation, highlighting their usefulness in tissue engineering.[3-5] Mesenchymal stem cells have already shown safety and efficacy in treating conditions like osteoarthritis, and their regenerative potential has paved the way for various cell-based therapies targeting a wide range of diseases.[6,7]

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Characteristic features of mesenchymal stem cells

Mesenchymal stem cells are mature, non-hematopoietic stem cells that possess multipotency and the ability to differentiate along mesodermal, ectodermal, and endodermal routes in addition to self-renewal.[8] These cells have the ability to develop into a variety of cell types, including chondrocytes, endothelial cells, osteoblasts, and cells that resemble neurons.[9] Gene-modified MSCs display characteristics such as directed migration, resistance to apoptosis, and selective tissue differentiation.[10] Research shows that MSCs from various tissues have comparable immunologic, differentiation capacity, and biological traits. MSCs possess the capacity to differentiate into neurons and astrocytes, as well as other mesenchymal and non-mesenchymal cell types.[11] After transplantation, MSCs retain their multipotential capacity and have distinct immunologic characteristics that allow them to remain in xenogeneic settings.[12] They are identified using surface markers like CD44, CD90, CD105, and others, and notably lack hematopoietic markers like CD34 and CD45.[13] In culture, MSCs display a fibroblast-like morphology and secrete

extracellular matrix proteins and paracrine factors that support tissue repair, underscoring their therapeutic potential.[14]

Sources of mesenchymal stem cells

Mesenchymal stem cells can be harvested from a variety of tissues, including bone marrow, adipose tissue, umbilical cord, and dental pulp. The most commonly investigated sources include bone marrow, adipose tissue, and perinatal tissues such as the UC and placenta.[15] Bone marrow-derived MSCs were the first to be identified and remain the classical reference population. However, their clinical use is limited by invasive harvesting procedures and relatively low cell yield.[16] Adipose-derived MSCs, by contrast, are abundant and can be obtained through less invasive methods like liposuction, offering similar regenerative capabilities.[17]

Perinatal sources, such as Wharton's jelly in the UC and placental tissue, provide cells with a more 'primitive' profile, potentially boosting their therapeutic effectiveness. It's essential to distinguish between hematopoietic stem cells from UC blood and MSCs from cord tissue to avoid scientific misinterpretation. The choice of MSC source can significantly impact cell behavior, including growth rates, differentiation capacity, and immune activity, making it a critical factor in both research and clinical applications.[18,19]

Applications of MSCs in tissue repair and regeneration

Thanks to their dual role in immune regulation and tissue regeneration, MSCs are central to advancing regenerative therapies.[20] Increasingly, their therapeutic value is attributed more to the molecules they secrete than to their ability to integrate into host tissues.[21] These secretions can stimulate healing by modulating immune responses and creating a pro-regenerative environment.[22] Notwithstanding their potential, practical uses need addressing obstacles, including the immune system's reaction to allogeneic cells.[23] Despite their promise, challenges remain, including immune reactions to donor cells and risks like unintended differentiation or tumor formation.[24] Mesenchymal stem cells are frequently used in bone repair therapies, but their regenerative potential can vary depending on the donor's age and other factors.[25] Predicting MSC populations' capacity for regeneration is difficult, nevertheless, due to their variability. Regenerative medicine faces both potential and challenges due to age-related alterations in MSC-derived exosomes and their molecular processes.[26,27] Studies have also explored their role in treating inflammatory conditions such as pancreatitis, supporting their therapeutic potential. With different countries adopting varying regulatory frameworks-Japan being a leader in approving MSC therapies-ongoing research continues to refine their use and ensure their safety in clinical settings.[26-28]

Mesenchymal stem cell-derived exosomes

Mesenchymal stem cells secrete a rich assortment of bioactive molecules-proteins, lipids, messenger RNAs (mRNAs), non-coding RNAs, and DNA fragments-which allow them to influence nearby cells.[29] This secretory function has led to growing interest in using MSCs for regenerative medicine, particularly through their exosomes.[30] These tiny vesicles act as biological messengers, facilitating cell-to-cell communication and enhancing tissue repair. Their therapeutic value is increasingly recognized, especially in animal models of disease.[31] While MSC-derived exosomes show immense potential in regeneration, more research is needed to fully understand their behavior in complex environments like tumors.[32] Identifying their molecular contents and standardizing production methods will be essential for reliable therapeutic applications. Aging and other factors may also affect the regenerative capabilities of these exosomes.[33]

Exosomes generated from MSCs have shown promise across various applications, including tissue regeneration, wound healing, immune modulation, and cancer therapy. They enhance the environment following myocardial infarction, support fracture healing, and may serve as a therapeutic option for brain cancers.[34-36] Exosomes secreted by MSCs can regulate key cellular processes, such as apoptosis in nucleus pulposus cells. This underscores their role in maintaining tissue balance and promoting repair. As a cell-free therapeutic approach, exosomes represent a highly attractive strategy

for addressing diverse pathological conditions and advancing tissue regeneration.[37]

EXOSOMES

Biogenesis

Exosomes are tiny extracellular vesicles, typically ranging from 30 to 150 nanometers in size, that are formed through the endosomal pathway. Their formation begins with the inward budding of the plasma membrane, which gives rise to early endosomes.[38] Subsequent invagination of the endosomal membrane results in the accumulation of intraluminal vesicles (ILVs) within multivesicular bodies (MVBs).[39] When MVBs fuse with the plasma membrane, ILVs are released into the extracellular space as exosomes. This process is tightly regulated by endosomal sorting complexes required for transport (ESCRT) as well as ESCRT-independent mechanisms involving tetraspanins and ceramide signaling.[40]

Exosomes exhibit a complex molecular composition that reflects the physiological state of their cell of origin. Their cargo includes proteins, lipids (cholesterol, sphingomyelin, ceramide), and nucleic acids such as mRNAs, microRNAs (miRNAs), and long non-coding RNAs (lncRNAs).[41] This selective enrichment in signaling molecules enables exosomes to act as carriers of functional information between cells. Importantly, the molecular profile of MSC-derived exosomes closely parallels that of their parental MSCs, particularly in relation to immunomodulatory and regenerative factors.[42]

Functions

Exosomes play pivotal roles in intercellular communication and exert diverse biological effects:

1. *Cell-cell communication:* Exosomes facilitate the transfer of bioactive molecules that influence gene expression and behavior in target cells.[43]
2. *Tissue repair and regeneration:* Mesenchymal stem cell-derived exosomes contribute to healing by promoting new blood vessel formation, inhibiting cell death, and stimulating cell proliferation in damaged tissues.[44]
3. *Immunomodulation:* Through the delivery of specific regulatory molecules such as programmed death ligand-1 (PD-L1) or certain miRNAs, exosomes can reduce inflammation and fine-tune T-cell activity.[45]
4. *Tumor microenvironment remodeling:* Exosomes secreted by tumor or supporting stromal cells can influence tumor progression by enhancing angiogenesis, evading immune surveillance, and promoting processes like epithelial-to-mesenchymal transition (EMT).[46]

Taken together, these roles establish exosomes as crucial mediators in both maintaining health and contributing to disease. Their dual nature, supportive in tissue repair yet potentially harmful in cancer development, emphasizes the need for context-aware assessment in their therapeutic use.

Physical characteristics of exosomes

Exosomes possess distinct physical properties that align with their function as vital mediators of intercellular signaling. Typically, they appear in cup-shaped or round morphologies and are enclosed by a lipid bilayer membrane that encapsulates a variety of biomolecules, including proteins, nucleic acids, lipids, and other essential components.[47] Accurately isolating and purifying exosomes, along with their cargo, is critical for both basic research and clinical studies.[48] A range of methods is available for exosome isolation, each offering different benefits and trade-offs in terms of yield, purity, and scalability. These include polymer-based precipitation, ultracentrifugation, size-exclusion chromatography (SEC), membrane filtration, and immunoaffinity capture.[49] Among these, ultracentrifugation remains one of the most commonly used techniques. However, due to the small size and low density of exosomes, this method can sometimes lead to reduced yields. In contrast, SEC has emerged as a promising alternative, demonstrating improved ability to preserve both the structural integrity and molecular content of exosomes.[50] Advanced separation technologies, especially SEC, are opening new avenues for refining exosome preparation. These methods enhance the quality and consistency of isolated exosomes, which are

essential for downstream analyses and potential therapeutic applications.[51]

Functions of exosomes in intercellular communication

Exosomes play a fundamental role in mediating communication between cells by acting as carriers of diverse molecular cargo, including proteins, lipids, nucleic acids, and other biologically active compounds.[52] Through this cargo exchange, they regulate numerous cellular processes and contribute to maintaining tissue and cellular homeostasis, especially in response to various physiological stresses.[53] Their involvement in paracrine signaling is particularly important for tissue repair, including processes like bone regeneration and fracture healing.[54] Research has shown that exosomes derived from MSCs actively support tissue regeneration by enhancing both osteogenesis and angiogenesis. In addition to bone-related healing, exosomes also contribute to cardiovascular repair by promoting angiogenesis and improving heart function following injury.[55,56] Beyond their regenerative capabilities, exosomes play critical roles in immune system function, inflammation, and immune regulation. They facilitate communication between immune cells and other cell types, thereby influencing immune interactions and responses.[57] In particular, stem cell-derived exosomes have demonstrated strong immunomodulatory properties, suggesting potential therapeutic applications for diseases involving immune dysfunction or imbalance.[58,59] As key mediators of cell-to-cell communication in tissue repair, exosomes contribute to the healing of peripheral nerves, the regeneration of skin and bone tissues, and improved wound healing outcomes. Their ability to deliver bioactive molecules directly to specific target cells enables them to accelerate tissue recovery and repair processes.[60]

Importantly, the influence of exosomes extends beyond cancer biology; they are also involved in immune regulation, tissue remodeling, and the molecular mechanisms that underlie the progression of various diseases. Their capacity to transfer functional molecules and modulate cellular activity highlights their central role in numerous biological contexts.[61]

Exosome-mediated signaling pathways

Exosomes include a protein called syntenin, which functions as an adapter molecule between transmembrane receptors and signaling pathways.[62] This affects how cells react when exosomes contact with cells. By transferring regulatory molecules, exosomes contribute to alterations in apoptosis induced by chemotherapeutic agents, redistribution of cell cycle phases, and reprogramming of gene expression. Among these, exosomal miRNAs targeting the phosphatase and tensin homolog (PTEN)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) axis are particularly important, as they govern autophagic flux and the regulation of cellular turnover.[63]

Exosomes have the impressive ability to affect gene expression, signaling pathways, and cell cycle dynamics. This changes how sensitive recipient cells are to chemotherapy and influences their reactions to external signals.[64] These extracellular vesicles can impact how cells behave and function by transporting mRNA, regulating gene expression, and modifying signaling networks within recipient cells.[65] Such modifications are crucial for determining cell fate and affecting various cellular functions.[66]

Cancer cells can release exosomes that activate signaling pathways in recipient cells, promoting tumor invasion and the spread of metastases.[67] These vesicles can also alter the transcriptional profiles and signaling processes of target cells, which contribute to both the onset and progression of the disease.[68] Besides their roles in cancer, exosomes released by supportive cells can affect immune responses by sending signals that activate natural killer cells and regulate other cell functions.

When exosomes interact with recipient cells, they cause changes in gene expression, communication inside the cell, and biological responses. Acting as dynamic signaling units in the extracellular space, exosomes influence cell behaviors through receptor engagement, the activation of signaling pathways, and genetic regulation. This ultimately has significant effects on both health and disease.[69]

Role of exosomes in health and disease

Exosomes exert profound effects on cellular equilibrium and have been associated with the pathogenesis of diverse conditions such as chronic inflammation, malignancies, and neurodegenerative syndromes. Acting as central messengers of intercellular communication, they modulate cell behavior and contribute to disease progression. In the respiratory system, the importance of exosomes is underscored by the role of exosomal miRNAs in maintaining pulmonary homeostasis and influencing the course of lung-related disorders.[70] Exosomal lncRNAs support oral tolerance and the function of the epithelial barrier in the intestinal mucosal immune barrier, hence underlining the importance of exosomes in immune regulation and helping to maintain homeostasis.[71] Exosomes produced from MSCs have demonstrated promise in controlling inflammatory reactions and maintaining joint health, which may lead to the treatment of osteoarthritis.[72] Evidence indicates that exosomal miR-146a, released from MSCs, potentiates the efficacy of sepsis therapies, thereby highlighting the central role of exosomes in regulating immune responses.[73] Exosomes have an effect on neurodegenerative diseases as well; exosomal miRNAs produced from MSCs are particularly relevant in neuroinflammatory pathways, indicating their potential for a range of neurological disorders.[74] Exosomes have been linked to the pathophysiology of neurodegenerative illnesses by facilitating the spread of genetic material and pathogenic proteins.[75] Exosomes play a dual role in inflammatory illnesses, serving as both possible therapeutic agents and mediators of inflammation. Immune cell exosomes have the capacity to exacerbate medical problems by acting as pro-inflammatory mediators, but they can also have therapeutic benefits due to their anti-inflammatory properties. Exosomes are adaptable intercellular communication mediators that affect physiological processes and have a role in the etiology of a number of disorders. Comprehending the functions of exosomes in preserving homeostasis and their engagement in pathological processes is vital for formulating focused treatment approaches and augmenting our comprehension of cellular communication pathways.[76]

Therapeutic potential of exosomes

Due to their special qualities, exosomes have drawn interest for their possible uses in drug delivery, regenerative medicine, and illness treatment. Exosomes produced from MSCs have shown restorative qualities in regenerative medicine, supporting angiogenesis, osteogenesis, and tissue regeneration.[77] Exosomes have been investigated as therapeutic agents without cells, and their potential for tissue repair and regenerative medicine is encouraging.[78] Their application in therapy could optimize treatment outcomes by improving drug bioavailability and lowering the risk of systemic adverse effects.[79] Exosomes have shown promise in the therapy of diseases such as neurological illnesses, inflammatory disorders, and cancer. Current evidence indicates that exosomes can influence pathological mechanisms in inflammation, cancer, and neurological disease.[77] Exosomes have the potential to be therapeutic, but their clinical translation is fraught with difficulties. Realizing the full potential of exosomes in clinical practice requires overcoming obstacles in clinical translation and learning more about their mechanisms of action.[78]

Exosomes and cancer progression

Exosomes secreted by tumor cells are increasingly recognized as key mediators of cancer progression. By transferring proteins, lipids, and nucleic acids, they orchestrate multiple processes within the tumor microenvironment and systemically, thereby facilitating tumor growth and metastasis.[80]

Epithelial to mesenchymal transition

One major mechanism by which exosomes contribute to malignancy is the induction of EMT. Exosomal cargo, such as transforming growth factor beta and specific miRNAs, can downregulate epithelial markers while upregulating mesenchymal markers. This phenotypic switch enhances cellular motility and invasiveness.[81] Importantly, cancer cells undergo loss of differentiation status, enabling them to acquire stem cell-like characteristics that facilitate metastasis.

Angiogenesis

Exosomes promote angiogenesis by delivering pro-angiogenic factors, including

vascular endothelial growth factor and angiogenesis-related miRNAs. These vesicles stimulate endothelial cell proliferation and migration, thereby establishing new blood vessels that provide nutrients and oxygen to expanding tumors.[82]

Immune modulation

Tumor-derived exosomes play an essential role in immune evasion. They may carry immune checkpoint molecules such as PD-L1, which suppresses T-cell activation, or release miRNAs that modulate macrophage polarization toward an immunosuppressive phenotype. By shaping the immune microenvironment, exosomes enable tumor cells to escape host immune surveillance.[83]

Pre-metastatic niche formation

Exosomes also contribute to the establishment of pre-metastatic niches in distant organs. They modify the extracellular matrix, recruit bone marrow–derived stromal cells, and condition local immune cells, thereby creating a permissive environment for metastatic colonization.[84]

Taken together, exosomes act as versatile mediators that influence virtually every stage of tumor progression, from local invasion and angiogenesis to systemic immune evasion and metastasis. A deeper understanding of these mechanisms not only clarifies the complex biology of cancer but also opens new avenues for developing exosome-based biomarkers and therapeutic strategies.

Exosomes and drug resistance

Although various anti-tumor agents have been developed in the field of cancer treatment, long-term use of these chemotherapeutic agents has been observed to cause drug resistance and an unfavorable prognosis.[85] Exosomes and cancer have been studied extensively, and their cargo delivery capacity has made them appealing candidates for chemotherapeutic uses. Recent research indicates that, due to their nanoscale structure, exosomes can act as carriers for the combination delivery of a miR-21 inhibitor and 5-fluorouridine (5-FU), potentially increasing the therapeutic impact against colorectal cancer. Using electroporation, researchers successfully contained both 5-FU and miR-21 inhibitors within exosomal vesicles. *In vivo* treatment of these modified exosomes in mice models resulted in considerable tumor shrinkage, which was linked to enhanced cellular uptake and miR-21 suppression. This dual delivery method enhanced apoptosis and cell cycle arrest, which were mediated through the up-regulation of tumor suppressor molecules such as PTEN and human mutS homolog 2, highlighting the translational importance of exosome-based therapeutics in colon cancer treatment.[86]

In pancreatic cancer, cancer stem cell-derived exosomes have emerged as key mediators of gemcitabine resistance. These vesicles contain miR-210, which activates mTOR-dependent pathways, inhibits apoptosis, and disrupts cell cycle regulation. Such interactions demonstrate how exosomes change signaling systems, reducing chemotherapeutic efficacy. Exosomes have been found to stimulate cisplatin efflux from ovarian cancer cells under hypoxic conditions and block the uptake of chemotherapeutic drugs.[87,88]

Effects of mesenchymal stem cell exosomes on cancer cells

Exosomes are essential in causing target cells to take on traits similar to those of cancer-associated fibroblasts (CAFs).[89] They have the ability to induce a more aggressive phenotype in both tumor and normal epithelial cells, which can result in increased motility, angiogenesis, and the acquisition of mesenchymal markers.[90] Exosomes generated from MSCs have been demonstrated to influence tumor progression by transferring certain miRNA species to adjacent cells, which in turn modulate tumor hallmarks.[91,92] Exosomes have been reported to exhibit bifurcating effects in cancer therapy: they can both inhibit the migration of glioma cells and their stem cell characteristics, while simultaneously stimulating the proliferation of tumor cells in gastric cancer.[93,94] Exosomes have demonstrated potential as drug delivery vehicles, improving treatment results for diseases such as hepatocellular carcinoma.[95] The potential of these exosomes to impede the growth of cancer cells through particular molecular processes, like downregulating Akt protein kinase phosphorylation, has been studied.[96] When utilized as a drug carrier system, they have been

investigated for their capacity to cause apoptosis and inhibit the signaling of the EMT in cervical cancer cells.[97]

Exosomes released by chronic lymphocytic leukemia cells have been shown to enable stromal cells to develop into CAFs, thereby creating a tumor-supportive environment that promotes cancer cell invasion and dissemination. Exosomes have been demonstrated to alter the tumor microenvironment and promote treatment resistance by controlling tumor cell proliferation, invasion, metastasis, and EMT.[98,99]

Mechanisms of MSC-derived exosomes on cancer cells

Exosomes produced from MSCs have been demonstrated to affect angiogenesis, immunological responses, and inflammatory processes inside the tumor microenvironment. These exosomes have a variety of effects on the course of cancer treatment and its outcome, including the ability to suppress tumor angiogenesis, modulate immune cell activity, and stimulate tissue regeneration. Through complex molecular pathways, MSC-derived exosomes are essential in mediating the effects of MSCs on cancer cells. Comprehending these pathways is crucial in order to leverage the therapeutic potential of exosomes produced from MSCs in cancer treatment and formulate focused approaches to impede the advancement and spread of disease.[100,101]

In order to modulate different cellular processes and facilitate intercellular communication, exosomes must engage and interact with cancer cells. Tumor-derived nanovesicles called exosomes are released by tumor cells and play a role in paracrine signaling that affects proliferative pathways, immunosuppression, and interactions between tumors and the stroma.[102] Cancer cells can internalize exosomes by a number of different processes, including as direct fusion with the plasma membrane, receptor-mediated endocytosis, and phagocytosis.[103,104]

Research has indicated that cancer cells have the ability to absorb exosomes produced by fibroblasts linked to cancer, which can change the behavior and characteristics of cancer cells.[105] In colorectal cancer, A disintegrin and metalloproteinase 17 located on the surface of exosomes can recognize and bind to integrin $\alpha5\beta1$ on target cells. This molecular recognition event plays a critical role in exosome internalization, thereby strengthening tumor-associated signaling.[106] It has been demonstrated that exosomes loaded with particular miRNAs promote the migration and proliferation of cancer cells when they are internalized by gastric cancer cells.[107]

It has been discovered that the blood-brain barrier is disrupted when exosomes produced from brain metastatic breast cancer cells internalize, since they carry certain long noncoding RNAs that alter the permeability of the barrier. Tumor growth and metastasis may be impacted by the internalization process, which may result in the transfer of oncogenes and oncoproteins throughout the tumor microenvironment and to other locations. The varied ways that exosomes containing particular epidermal growth factor receptor ligands promote invasiveness in breast cancer cells indicate that internalization of exosomes originating from cancer is associated with enhanced cancer cell invasion. These results highlight the role that exosome internalization plays in influencing the behavior of cancer cells and encouraging the growth of tumors.[108,109]

Numerous investigations have illuminated the various mechanisms and elements impacting cancer cells' ability to detect and absorb exosomes. The pH level of the microenvironment is one important factor affecting exosome uptake, as shown by. They demonstrated that low pH levels enhance exosome release and absorption, pointing to a possible function of pH in regulating exosome traffic and uptake. Emphasized the necessity of particular cell surface components in promoting exosome uptake and highlighted how cancer cell exosomes are dependent on cell-surface heparan sulfate proteoglycans for internalization.[110,111]

Showed that caveolin-1 adversely regulates the process of lipid raft-mediated endocytosis, which is how mammalian cells take up exosomes. This discovery sheds light on the biological processes behind exosome

internalization. Indicated the involvement of particular molecular interactions in the internalization process by implying that glycan-lectin interactions may be involved in exosome uptake by ovarian cancer cells. The processes via which cancer cells sense and absorb exosomes are largely dependent on the intricate interactions between a number of variables, such as pH levels, chemicals on the cell surface, lipid rafts, and receptor-mediated endocytosis. Comprehending these molecular pathways is essential to clarifying the dynamics of exosome-cell interactions and their consequences for the advancement of cancer and therapeutic interventions.[112,113]

Clinical applications of MSC-derived exosomes

Mesenchymal stem cell-derived exosomes have attracted increasing attention as cell-free therapeutic agents, largely since they reproduce many of the regenerative and immunomodulatory effects of their parental cells while avoiding risks associated with direct MSC transplantation, such as uncontrolled differentiation or tumorigenesis. Their stability, nanoscale size, and ability to cross biological barriers further support their potential for clinical use.[114]

Regenerative medicine

Exosomes derived from MSCs have demonstrated the capacity to promote tissue repair in preclinical models of cardiovascular, neurological, and musculoskeletal diseases. By delivering pro-angiogenic and anti-apoptotic factors, they enhance neovascularization, reduce cell death, and stimulate the proliferation of resident progenitor cells. In ischemic heart disease, for example, MSC-derived exosomes improved cardiac function by fostering angiogenesis and limiting fibrosis.[115,116]

Immunotherapy and inflammatory diseases

The immunomodulatory properties of MSC exosomes make them promising candidates for treating immune-related disorders. They can suppress T-cell growth, encourage regulatory T-cell differentiation, and change macrophage polarization. Early clinical studies have looked into their use for conditions like graft-versus-host disease and autoimmune disorders. The results have shown encouraging safety and effectiveness.[117]

Cancer therapy

While exosomes may help tumors grow, they also have the potential to treat cancer when engineered to deliver anti-cancer molecules. Modified MSC-derived exosomes have been used as carriers for miRNAs, small interfering RNAs, or chemotherapy drugs. They achieve targeted delivery to tumor cells while reducing overall toxicity. These methods show the dual nature of MSC exosomes. Careful design is needed to maximize their therapeutic benefits without worsening cancer.[118]

Biomarkers and diagnostics

Exosomes are valuable sources of biomarkers for disease diagnosis and prognosis due to their molecular cargo. Mesenchymal stem cell-derived exosomes found in patient biofluids can reflect the condition of the tissue microenvironment. This offers chances for minimally invasive monitoring of disease progression or response to treatment.[118]

Future perspectives

Although preclinical data are promising, several challenges remain before MSC exosomes can be fully used in clinical practice. We need to standardize isolation and characterization methods, produce them on a large scale, and evaluate their effectiveness in randomized clinical trials. Tackling these issues will be key to turning experimental findings into approved treatments.[119,120]

In conclusion, the role of MSC-derived exosome vesicles in cancer biology is rapidly increasing and expanding. In addition to their roles in cancer biology, such as angiogenesis, resistance, and immune evasion, exosomes also carry therapeutic potential as anti-tumor agents. Thus, exosomes possess dual characteristics and are important in this module of sensitive communication and complexity. Current studies should prioritise standardising isolation procedures, molecular mechanisms, and the efficacy and safety profiles of clinical applications for future studies. It is evident that fundamental biology and translational medicine

will collaborate to develop therapeutic strategies for MSC-derived exosomes. Their integration into clinical trials and applications could establish a balance by slowing tumor formation and enhancing immunomodulatory properties.

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