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Exosomes - breakthrough in the regenerative medicine and a way to improve the quality of the life

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ABSTRACT

Introduction

Exosomes are small, membrane-bound extracellular vesicles that play a pivotal role in intercellular communication. Exosomes have garnered significant interest in regenerative medicine due to their unique properties that support tissue repair, regeneration, and healing. These extracellular vesicles play a crucial role in intercellular communication, and their regenerative potential makes them promising tools in the field of regenerative medicine.

Purpose of the study

This review aims to present the regenerative properties of exosomes and their clinical applications in many fields of medicine. The main aim is to present exosomes as a substance that restores health, youth and vitality.

Material and method

Literature review was primarily based on scientific materials, English and Polish databases and original research. The following English keywords and its Polish equivalents were used to search Google Scholar and PubMed: “ exosomes", “regenerative medicine”, “stem cells”.

Key words

exosomes, regenerative medicine, stem cells

Introduction

Definition and biogenesis of exosomes

Exosomes are small, membrane-bound vesicles secreted by cells into the extracellular space. These tiny structures, ranging from 30 to 150 nanometers in diameter, play a crucial role in intercellular communication and the transfer of biological information between cells. Exosomes are generated by various cell types, including immune cells, neurons, stem cells, and cancer cells, and they are found in various bodily fluids such as blood, urine, and saliva. [1] Exosomes are formed through the endocytic pathway. Early endosomes mature into multivesicular bodies (MVBs), and intraluminal vesicles (ILVs) are created within these bodies. When MVBs fuse with the cell membrane, ILVs are released into the extracellular space as exosomes.[2] Exosomes carry a cargo of bioactive molecules, including proteins, lipids, and nucleic acids. The specific composition of exosomes depends on the cell type of origin and their physiological or pathological state. Common proteins found on exosome surfaces include tetraspanins (CD9, CD63, CD81), Alix, and TSG101. [1,2] The biogenesis of exosomes is a complex and highly regulated process involving the endosomal sorting complex required for transport (ESCRT) machinery, lipids, and various proteins. Exosomes originate from the endocytic pathway, where portions of the cell membrane are engulfed and internalized to form early endosomes. These early endosomes undergo maturation to become multivesicular bodies (MVBs), which eventually release exosomes into the extracellular space. The biogenesis of exosomes can be summarized in several key steps. [3] The process begins with endocytosis, during which the cell membrane invaginates to form early endosomes. These early endosomes contain materials internalized from the cell surface, including membrane proteins, extracellular fluids, and other molecules. [3,4] Early endosomes mature into multivesicular bodies (MVBs) through a process involving the ESCRT machinery. The ESCRT machinery consists of four protein complexes: ESCRT-0, ESCRT-I, ESCRT-II, and ESCRT-III that work together to facilitate the formation of intraluminal vesicles (ILVs) within the MVBs. The ESCRT-dependent pathway involves the recognition of ubiquitinated proteins on the endosomal membrane by ESCRT-0. This initiates a series of events where ESCRT-I and ESCRT-II are recruited, leading to the budding of ILVs into the MVB. ESCRT-III is then recruited to complete ILV formation. In addition to the ESCRT-dependent pathway, there is an ESCRT-independent pathway involving lipid raft microdomains and tetraspanins. Lipid rafts are regions of the membrane enriched in cholesterol and sphingolipids. Tetraspanins, such as CD9, CD63, and CD81, interact with lipids and other proteins, facilitating the assembly of exosomes. [5] During the formation of ILVs, specific cargo molecules, including proteins, lipids, and nucleic acids, are selectively incorporated into the vesicles. This cargo can include signaling molecules, receptors, microRNAs, and various bioactive molecules. [3,5] Mature MVBs containing ILVs have two potential fates. They can either fuse with lysosomes for degradation, leading to the breakdown of the cargo, or they can traffic to the cell surface for exosome release. MVBs that are destined for exosome release move towards the cell membrane and fuse with it, releasing the ILVs into the extracellular space as exosomes. This fusion is facilitated by SNARE proteins, which are involved in vesicle trafficking and membrane fusion. Once released, exosomes can travel to nearby or distant cells, where they are taken up by recipient cells. This internalization can occur through various mechanisms, including endocytosis, phagocytosis, or direct membrane fusion. Understanding the biogenesis of exosomes is crucial for unraveling their roles in intercellular communication, health, and disease. The dynamic and regulated nature of exosome biogenesis underscores their importance in facilitating cellular communication and maintaining cellular homeostasis. [6,7]

The multiple functions of exosomes

Exosomes serve diverse functions in intercellular communication, playing critical roles in both physiological and pathological processes. These small extracellular vesicles are released by various cell types and carry a cargo of proteins, lipids, and nucleic acids, including microRNAs and mRNAs. Exosomes act as messengers in intercellular communication by transporting bioactive molecules from donor cells to recipient cells. They facilitate the exchange of information between different cell types and tissues. [8] Exosomes play a crucial role in immune regulation. They can modulate immune responses by carrying signaling molecules, antigens, and immune-regulatory factors. Exosomes derived from immune cells influence the activation, differentiation, and function of other immune cells. [9] Exosomes participate in the removal of cellular waste and obsolete cellular components. They contribute to maintaining cellular homeostasis by facilitating the elimination of unnecessary or damaged cellular materials. [10] In the nervous system, exosomes play a role in neural communication. They transport signaling molecules, growth factors, and genetic material between neurons and glial cells, influencing synaptic function, neuroprotection, and responses to injury. [11] Exosomes carry genetic information in the form of microRNAs, mRNAs, and other nucleic acids. This transfer of genetic material can influence gene expression and cellular function in recipient cells. [11,12] In the cardiovascular system, exosomes contribute to vascular function and homeostasis. They can influence endothelial cell function, vascular tone, and angiogenesis, playing roles in both health and disease. [13] Tumor-derived exosomes are implicated in cancer progression. They can promote angiogenesis, immune evasion, and the preparation of distant sites for metastasis. Exosomes derived from cancer cells contribute to the communication within the tumor microenvironment. [14] Exosomes may participate in hormonal signaling by carrying hormones, hormone receptors, or molecules involved in hormonal pathways. This allows for the exchange of signaling information between cells and tissues. [15,16] Exosomes are explored as potential diagnostic biomarkers for various diseases. The presence of specific molecules or genetic material within exosomes can provide information about the physiological or pathological state of cells and tissues, aiding in disease diagnosis and monitoring. [16, 17] Furthermore exosomes are being investigated for their therapeutic potential. They can be engineered to carry therapeutic cargo, such as drugs or genetic material, making them promising candidates for drug delivery and regenerative medicine applications. Understanding the multifaceted functions of exosomes is essential for advancing research in areas such as regenerative medicine, cancer biology, immunology, and neurobiology. The ability of exosomes to mediate cellular communication highlights their significance in maintaining tissue homeostasis and influencing various physiological and pathological processes. Exosomes, particularly those derived from stem cells, contribute to tissue repair and regeneration. They stimulate cell proliferation, angiogenesis, and tissue remodeling, promoting the healing of damaged tissues. [18]

Exosomes vs Stem cells

Exosomes and stem cells are distinct entities, but they share a close relationship, particularly in the context of regenerative medicine. Firstly distinguished by nature and composition. As above it has already been describedExosomes are small extracellular vesicles released by cells. They are membrane-bound structures ranging from 30 to 150 nanometers in diameter.

Exosomes contain a cargo of bioactive molecules, including proteins, lipids, and nucleic acids. Stem cells are undifferentiated cells with the potential to differentiate into various cell types. They can be categorized into pluripotent, multipotent, and unipotent stem cells based on their differentiation potential. [19] The second difference that distinguishes exosomes from stem cells may be the function of both of them. Exosomes primarily serve as vehicles for intercellular communication. They transfer information in the form of their cargo from donor cells to recipient cells, influencing cellular processes such as proliferation, differentiation, and immune responses. [9,20] Stem cells have the unique ability to self-renew and differentiate into specialized cell types. They play a central role in tissue regeneration, repair, and maintenance. Stem cells contribute to the replacement of damaged or aged cells in various tissues and organs. Further difference can be regenerative potential. [21] Exosomes derived from stem cells, often referred to as "stem cell-derived exosomes," contribute to the regenerative potential associated with stem cell therapies. These exosomes can carry regenerative signals and bioactive molecules that promote tissue repair and regeneration. The regenerative potential of stem cells lies in their ability to differentiate into specific cell types required for tissue repair. Stem cell therapies aim to harness this regenerative capacity to treat various diseases and injuries. [22] Exosomes and stem cells also differ in terms of clinical application. Exosomes are being actively explored for therapeutic applications, including regenerative medicine and drug delivery. They offer a cell-free alternative to traditional stem cell therapies and may provide targeted delivery of therapeutic cargo.[23] Stem cell therapies involve the direct transplantation or injection of stem cells into a patient to replace or repair damaged tissues. These therapies are being investigated for conditions such as heart disease, neurodegenerative disorders, and musculoskeletal injuries. [24] Another difference is mechanism of action. Exosomes the therapeutic effects of exosomes are mediated by the transfer of their cargo to recipient cells. This cargo can include growth factors, signaling molecules, and genetic material, influencing cellular behavior.[1,6] Stem cells contribute to tissue repair through their differentiation into specialized cell types. They also secrete paracrine factors that promote the survival and function of surrounding cells.[25] Finally exosomes and stem cells can be differentiated according to the size and physical characteristics. Exosomes are nanosized vesicles with a lipid bilayer membrane. Their small size allows them to traverse biological barriers and reach target cells.[1,7] Stem cells are typically larger than exosomes and have a cellular structure. They can be isolated as single cells or cultured in vitro to expand their numbers.[1,26] While exosomes and stem cells have distinct characteristics, their functional interplay is of great interest in regenerative medicine.

Exosomes derived from stem cells harness the regenerative signals of stem cells in a cell-free form, offering potential advantages in terms of safety, storage, and targeted therapeutic delivery. Both exosomes and stem cells contribute to the evolving landscape of regenerative and personalized medicine.

Role of exosomes in Sports Medicine

Exosomes are gaining attention in the field of sports medicine for their potential applications in injury recovery, tissue regeneration, and overall performance enhancement. Exosomes, particularly those derived from mesenchymal stem cells, have regenerative properties that can aid in the recovery from sports-related injuries. These tiny vesicles can promote the regeneration of damaged tissues, including muscles, tendons, and ligaments. The regenerative signals carried by exosomes may accelerate the healing process, helping athletes recover more efficiently. Exosomes derived from muscle cells or stem cells have the potential to stimulate muscle repair and regeneration. This property is of interest in sports medicine for athletes looking to enhance muscle recovery and optimize performance. Exosomes may influence muscle cell proliferation and differentiation, supporting the development of healthy muscle tissue. Tendon and ligament injuries are common in sports, and their healing can be challenging. Exosomes, especially those derived from MSCs, may play a role in promoting the repair of tendon and ligament tissues. The regenerative signals carried by exosomes can influence the behavior of cells involved in tissue healing. [27] Exosomes have been shown to have anti-inflammatory effects, modulating the immune response. In sports medicine, this property is relevant for managing inflammation associated with injuries or overexertion. Exosomes may help control excessive inflammation, contributing to a faster and more controlled healing process. Exosomes have been investigated for their potential in promoting cartilage regeneration. In sports medicine, where joint injuries and cartilage damage are prevalent, exosomes may offer a non-invasive and regenerative approach to support cartilage repair and prevent the progression of degenerative joint conditions. [28] Exosomes may have analgesic effects, contributing to pain management in sports-related injuries. By modulating inflammation and promoting tissue repair, exosomes could potentially alleviate pain associated with injuries or chronic conditions. Integrating exosome-based therapies into rehabilitation protocols may enhance the overall recovery process for athletes. Whether recovering from surgery or managing overuse injuries, exosomes could be utilized to optimize tissue healing and minimize downtime. Exosomes offer the potential for personalized medicine approaches in sports. Tailoring exosome therapies to individual athletes based on their specific injury, genetic factors, and response to treatment could optimize outcomes and minimize the risk of complications. [29] While the field of exosomes in sports medicine is still in the early stages of research, the regenerative and anti-inflammatory properties of exosomes make them promising candidates for novel therapeutic approaches. Clinical trials and further research are needed to establish the safety and efficacy of exosome-based treatments in the context of sports-related injuries and performance optimization.

Regeneration properties of the exosomes in few fields of medicine

Exosomes have gained significant attention in various fields of medicine due to their role in intercellular communication and their potential therapeutic applications. Exosomes are central to regenerative medicine due to their ability to modulate cell behavior and tissue repair. Stem cell-derived exosomes, in particular, have regenerative properties. They can stimulate the proliferation and differentiation of endogenous stem cells, promoting tissue regeneration in various organs and systems. Exosomes are being investigated for their role in cancer progression and as potential therapeutic tools. They can carry oncogenic factors, promoting tumor growth, but they also have the potential for targeted drug delivery. Researchers are exploring exosome-based therapies for cancer treatment, such as delivering anti-cancer drugs or using engineered exosomes to stimulate the immune system against cancer cells. [30] In neurology, exosomes are studied for their involvement in neurodegenerative diseases such as Alzheimer's and Parkinson's. They play a role in the spread of misfolded proteins implicated in these disorders. Additionally, exosomes derived from stem cells or neural cells show promise in promoting neural regeneration and functional recovery after injuries or degenerative conditions. [31] Exosomes have implications in cardiovascular diseases. They participate in cardiac regeneration by promoting angiogenesis, reducing inflammation, and influencing the behavior of cardiac cells. Researchers are exploring exosome-based therapies for myocardial infarction and heart failure, aiming to enhance cardiac repair and function. [32] Exosomes play a role in immune system regulation and response. They can carry signals that modulate immune cell activity, influencing both innate and adaptive immune responses. Exosomes are being explored as potential immunotherapeutic agents, either as vaccines or as tools to modulate immune responses in conditions such as autoimmune diseases. [33] In infectious diseases, exosomes are studied for their involvement in host-pathogen interactions. They can carry viral or bacterial components, influencing the immune response. Researchers are exploring whether exosomes can be used to develop diagnostic tools or therapeutic interventions for infectious diseases. [34] In orthopedics, exosomes are investigated for their potential in promoting musculoskeletal tissue regeneration. They can influence the behavior of osteoblasts and chondrocytes, contributing to bone and cartilage repair. Exosome-based therapies are being explored for conditions such as osteoarthritis and bone fractures. [35] Exosomes are also gaining attention in the field of aesthetic medicine for their potential in skin rejuvenation, anti-aging, and hair restoration. Exosomes derived from mesenchymal stem cells (MSCs) have shown promise in promoting skin rejuvenation. They carry growth factors, cytokines, and other signaling molecules that can stimulate collagen production, improve skin elasticity, and enhance overall skin quality. Exosome-based therapies may be used to address fine lines, wrinkles, and sun-damaged skin. [36] Exosomes play a role in wound healing by promoting cell migration and tissue regeneration. In aesthetic medicine, they may be used to accelerate the healing process after procedures like laser treatments or chemical peels, reducing downtime and minimizing scarring. [36, 37] Exosomes are being investigated for their potential in treating hair loss and promoting hair regrowth. They can influence the activity of hair follicle cells, stimulate angiogenesis in the scalp, and modulate inflammation, all of which are relevant factors in hair restoration. Exosome-based therapies may complement existing treatments for conditions like alopecia. [38] In procedures involving fat grafting or tissue augmentation, exosomes may enhance the survival and integration of transplanted cells. Exosomes derived from adipose-derived stem cells, for example, can carry factors that support tissue regeneration, contributing to better outcomes in aesthetic procedures. [39] Exosomes possess anti-inflammatory properties, which can be beneficial in managing inflammatory skin conditions. In aesthetic medicine, this can be relevant for addressing redness, swelling, and irritation associated with certain procedures or skin conditions. [40] Exosomes can carry factors that stimulate the production of collagen, a key protein for maintaining skin structure and firmness. This property is valuable in aesthetic treatments aiming to improve skin texture and reduce the signs of aging. [41] Cosmetic companies are exploring the development of topical skincare products containing exosomes. These products are designed to deliver exosome-derived factors directly to the skin, providing a non-invasive approach to harnessing the regenerative properties of exosomes for aesthetic purposes. [42] While research in the aesthetic application of exosomes is still in its early stages, preliminary studies and clinical trials suggest promising results. As the understanding of exosome biology advances, it is likely that exosome-based therapies will become increasingly integrated into aesthetic medicine for their regenerative and anti-aging potential. However, it's important to note that regulatory approval and further research are needed to establish the safety and efficacy of these treatments in aesthetic applications. These examples illustrate the diverse applications of exosomes in medicine, reflecting their role in cellular communication and their potential as therapeutic tools in various medical fields. Ongoing research continues to uncover new possibilities and refine our understanding of exosome-based approaches in healthcare.

Conclusion

Exosomes derived from various cell types are being explored for their potential in cardiovascular health. They may influence factors such as angiogenesis, vascular function, and tissue repair, contributing to overall cardiovascular well-being. While the direct impact of exosomes on mental health is an area of ongoing research, the potential for exosomes to modulate cellular responses to stress may indirectly contribute to mental well-being. Managing cellular stress is crucial for overall health, including mental health. Exosomes may offer personalized therapeutic approaches. By tailoring exosome-based therapies to an individual's specific health conditions and needs, healthcare providers can potentially optimize treatment outcomes and enhance the overall quality of life for patients. It's important to note that while exosomes show promise in various aspects of regenerative medicine, more research and clinical studies are needed to fully understand their therapeutic potential and establish their safety and efficacy in different contexts. As the field continues to advance, exosome-based therapies may contribute to improving the quality of life for individuals facing a range of health challenges.

Author's contribution

For full transparency, all submitted manuscripts must include an Author Contribution Statement stating the work of each author. For research articles with multiple authors, a short paragraph must be provided stating their individual contributions.

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Disclosure

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