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Exosomes and their function

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Abstract

Exosomes are structures that carry small molecules such as peptides, RNA, and DNA for different functions in our system. They have a role as intercellular transmission and transfer agent. They provide the protection of homeostasis through these transmission activities. They are involved in the pathogenesis of many different disorders such as cancer, neurodegenerative, cardiovascular and infectious diseases. Exosomes have great importance in the diagnosis of the clinical diseases as biomarker carriers. In this way, they enable early diagnosis and treatment for the patients. Common techniques used today when isolating exosomes are differential ultracentrifugation and exosome purification. In this study, we will review exosomes and their importance in different diseases.

Introduction

Exosomes are vesicles secreted from cells [1]. Exosomes are small nano-sized (30-100nm) arrays with a lipid cell membrane that are secreted in all cell types [1]. Exosomes released by all cells that are involved in biological activities such as intracellular communication, signal transduction, molecular transfer and immune response [2]. Microvesicles are formed by the development of the buds from the cell membrane towards outside. They are formed by the budding of the exosomes from the cell [3].

Exosomes provide extracellular delivery of intercellular lipids,non-coding RNA such as miRNA and circRNA, mRNA and DNA *in vitro* and *in vivo*. These structures contain cytosolic and nuclear proteins [2]. They can be secreted from the cell in two ways; as constitutive and stimulatory. Structural secretion is regulated by certain RAB GTPases, glycosphingolipids and flotilins. The last common step in the secretion of the exosomes in constitutive and stimulatory release, is the integration of the microvessels with the plasma membrane [2,3].

It is secreted by different cell types such as mast cells, lymphocytes, epithelial cells, dendritic cells, thrombocytes, endothelial cells and neurons [3-5]. Exosomes send specific interactions and signals to each cell. For example, it results in the activation of the downstream signaling in ligand-receptor interaction [2]. Exosomes are classified as microvesicles, apoptic bodies or exosomes, depending on their size and biogenesis [5]. Exosomes are involved in the immune system by completing antigen presentation, immune activation, and immunosuppression [2,4].

While isolating the exosomes methodology depends on different factors such as: morphology, buoyancy consistency and the construction of the marker proteins for example Alix, TSG101, flotillin 1, HSP70 and CD9. The following techniques are generally used during their isolation process: Differential centrifugation, size exclusion chromatography, immune affinity capture, commercially available kits or microfluidic technologies [3,6]. The most common of the above techniques that is used when isolating the exosomes is; differential ultracentrifugation [3,6].

Results

Exosomes can get involved in the pathogenesis of versatile diseases such as diabetes, cardiovascular disease, endothelial dysfunction, coagulopathies, cancer, neurodegeneration and polystic ovary syndrome [5,8].

Exosomes have utilization in cancer detection; they are detected in the biological fluid samples such as urine, semen, saliva, amniotic fluid, cerebrospinal fluid, bile, acid, tears, breast milk and blood [8]. They transmit nucleic substances and proteins from the host cells. For example, tumor cells secrete exosomes containing tumor-specific RNAs that can be used for the cancer diagnosis [8]. In cancer, exosomes are mostly defined as factors that reinforce tumor progression. In addition, some studies suggests that exosomes can also have antitumor properties [2,8]. Depending on the content they carry they can have either tumor promoting or suppressing roles.

It has been shown that tumor immune-derived exosomes carry tumor antigens and support immunity, and this leads to the destruction of the tumors via CD8-T cells. In addition, through the signals they recieve from exosomes, CD4-T cells are thought to show resistance to tumor growth and tumor development [8].

In order for the cancer treatments to result in effective outcomes, the drugs used must be delivered to tumor cells quickly and accurately. Exosomes, called biomarkers, offer promising treatments with nanotechnology-based drug delivery systems. Exosomes are used effectively in cancer therapy and as RNA delivery vectors by using their natural distribution capabilities when they are present in a wide range of biological fluids [3,8].

Signal transmission between cells in the heart is regulated by the fibroblasts, endothelial cells and cardiomocytes [9]. This regulation leads to cardiac remodeling [9]. By measuring endothelial microvesicles,, patients who are vulnerable to coronary heart disease can be identified [6]. Some studies showed that exosomes are involved in cardiovascular diseases including but not limited to cardiomyocyte hypertrophy, periportum cardiomyopathy and cardiomyopathy.[9] Natural distribution ability, small size and easy accessibility suggest that exosomes can play a major role in the treatment of the heart diseases. However, studies are still ongoing for this type of treatment [9,10].

Discussion

The main known role of exosomes is the removal of the intact endosomal proteins and cell membranes. Exosomes are well tolerated by the body since they are not recognized as foreing since they can be formed by all type of cells, resemble cell membranes, and can cross obstacles such as blood brain barrier [11]. Exosomes are mostly known for their anti-tumor activities by suppressing the immune reaction against the tumor cells [12]. Most of the studies focus on their utilization as early cancer diagnosis markers [3,6].

Exosomes are also involved in the pathogenesis of cancer, neurodegenerative and cardiovascular diseases. Recent studies have proven that exosomes play an important role in the development of the infectious diseases. In addition, some other studies showed that hepatitis B, C and E viruses use the exosomal pathway mechanism to transmit disease persistence [13,14]. It is very important to diagnose clinical diseases through exosomes for such diseases. However, clinical applicability is limited due to the standard isolation and purification technologies [13].

Conclusion

New studies are needed for the development of effective treatment methods against infectious diseases, cardiovascular and neurodegenerative disorders. Exosomes can be great candidates as early diagnosis markers besides their utilization as peptide, non-coding RNA and DNA carriers to cure certain disorders. Although exosomes have been mostly studied in areas such as cell biology and biomedicine, recent studies have determined that they can be utilized in industries such as food and agriculture [11]. More studies should be conducted to determine the efficacy and safety of the exosomes as delivery agents for different purposes.

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