Review

Research progress on the function and mechanism of exosomes

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Abstract

Exosomes are involved in a variety of functions such as immune response and tumor invasion. Exosomes have been shown to be related to the mechanism of action in the occurrence and development of a variety of diseases. In this paper, the production, transport and release process of exosomes are briefly described, and the biological significance behind them is expounded. The role of exosomes in these diseases is also discussed from the perspectives of infection, senescence and tumor.

Keyword

Exosome; infection; senescence; tumor; mechanism;

Introduction

Exosomes are polyvesicles (MVBs) with an average size of 100 nm formed from small extracellular vesicles (sEV). By means of budding, the intrinsic components are transported to the extracellular environment and released, in which the components can change the local microenvironment or interacts with the target cells to activate the

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signal pathway in the target cells. Exosomes contain a variety of transport molecules, including lipids, proteins, DNA, RNA, mRNA, miRNA, etc[1]. Exosomes are found in body fluids, including blood, saliva, urine, cerebrospinal fluid, and milk. Almost all cells can secrete exosomes under physiological conditions. Interestingly, the composition and secretory mode of exosomes will change under pathological conditions. Therefore, exosomes play an important role in the occurrence, development and outcome of diseases. The study of exosomes contributes to the understanding of the pathophysiological mechanisms of disease. And it has the potential to be a good biomarker in clinical application because of its changing properties.Some researchers believe that exosomes can be used as a treatment for diseases, based on their ability to regulate signaling pathways.

1.Formation, transport and release of exosomes

Endosomes are formed by membrane invagination of internal cells. The early endosomes may fuse with the endocytic vesicles. The contents to be recycled are classified as recycled interiors. The remaining early endosomes are transformed into late endosomes. Late endosomal accumulation of ILV formed by endosomal membrane budding inward. During this process, cytoplasmic proteins, nucleic acids and lipids are sorted into these

vesicles. Advanced endosomes containing a large number of small vesicles are called MVB. Formation of Intracavitary vesicles (ILV) requires two distinct processes. First, the endosomal membrane is reorganized so that it is highly enriched with tetratrans proteins. Endosomal sorting complexes (ESCRTs) required for transport are recruited to the ILV formation site and influence the endosomes to release them into the extracellular space. Exosomes are released by MVB membrane fusion with plasma membrane. The Extracellular vesicles（EV） membrane surface can trigger signal transduction by interacting with receptors/ligands on the cell surface. In most cases, the function of EV contents depends on entering the cytoplasm and possibly even the nucleus. Different cell types are able to use various mechanisms to absorb EV, resulting in functional transfer of cargo or degradation of EV content[2].

2.Virus infection and exosomes

Exosomes have the ability to transport contents such as nucleic acids and proteins to other cells. This provides a new way of transferring materials between cells. At the same time, it also AIDS the transfer of viral nucleic acids and proteins from cell to cell. Various enveloped viruses can hijack the exosome ESCRT system to assist virus proliferation, budding, and transmission[3]. Non-enveloped viruses acquire host-derived membranes for

cell-to-cell transmission, and the viruses are still able to replicate in recipient cells. Therefore, the ESCRT system has become an indispensable tool for enveloped virus infection. Retroviruses use exosome formation and release pathways in host cells to produce infectious virions. In viral infections, exosomes play a dual role in the regulation of the immune system, both as host programs that induce innate and adaptive immunity and as viral strategies to evade these same responses [4].

3.Aging and exosomes

Senescent cells also increase the secretion of a class of extracellular vesicles called exosomes. Decreased exosome secretion induces reactive oxygen species (ROS) -dependent DNA damage responses (DDR) in both senescent and non-senescent cells. The accumulation of DNA damage can lead to apoptosis or cell senescence[5]. Exosomes of damaged cells, including those rich in DNA damage markers (such as γH2AX and fragment telomere repeat DNA), can induce inflammation [6] .Exosomal miRNA are involved in the regulation of vascular aging by participating in the physiological function of vascular cells and the destruction and remodeling of extracellular matrix (ECM)[7]. The accumulation of substances in cells is mainly caused by the reduced transport efficiency of substances. DNA secretion of cells provides a new way for senescent

cells to expel excess DNA, which is of great significance for maintaining cell homeostasis. The excreted DNA-rich secretory, however, triggers an inflammatory response that promotes ageing. In addition, secretory bodies are also involved in the destruction of blood vessel cells and the regulation of aging of muscle cells and bone cells.

4.Tumors and exosomes

Exosomes not only transfer between cancer cells, they also transfer between cancer cells and stromal cells: stromal cells receive exosomes from cancer cells and produce tumor-promoting microenvironments; In turn, cancer cells release exosomes from stromal cells to promote cancer cell proliferation or invasion. It is well known that VEGF is closely related to the occurrence and development of tumors. Exosomes promote angiogenesis by regulating endothelial cell characteristics. Under hypoxia conditions, exosomes can promote tumor growth by increasing angiogenesis. In addition, exosomes have a strong influence on drug resistance and induce resistance through a variety of mechanisms. Exosomes control cell polarity and directed cell movement, which are closely related to tumor cell metastasis. Exosomes can also cause a strong pro-tumor immune response[8]. Fibroblasts, endothelial cells and infiltrating immune cells are the main cell types that interact with tumor cells through exosome

signaling in the tumor microenvironment. These cellular interactions affect exosome composition and quantity. Stress conditions such as hypoxia, starvation and acidosis can increase exosome release in malignant cells [9].

Conclusion

In this paper, we briefly describe the biological processes of exosome production, transport and release. The molecular mechanisms of infection, senescence and tumor were explored based on the biological processes of exosomes. This gives us insight into the pathophysiological processes of disease. Exosomes have a good biological application prospect, both as biomarkers and therapeutics, showing great biological prospects.

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