Mini Review

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Exosomal MIRNAS and cancer

Abstract

MicroRNAs (miRNAs) represent a large family of small, nearly 20-22 nucleotides non-coding RNAs that modulate the expression of target genes, especially at the post-transcriptional level. Many studies suggest that miRNAs play a role in homeostatic preservation and that deviant expression of miRNAs is usually seen in several types of diseases, such as cancer. Exosomes are extracellular vesicles synthesized in the cells. They induce cell-cell communication and immunoregulatory functions. In cancer, exosome secretion is associated with primary tumor growth, regulation of local tumor microenvironment, and stimulation of distant metastatic niche formation during tumor spread. MiRNA expression is often dysregulated in tumour cells and can be reflected by distinct exosomal miRNA (ex-miRNA) profiles isolated from the cancer patients. In this minireview, we sum up the current understanding about exosomal miRNAs (ex-miRNAs) functions in cancer. We also review the possible clinical utilization of ex-miRNAs in cancer, for instance as diagnostic marker and therapeutic target.

Keywords: microrna, exosomes, cancer, marker

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Introduction

MicroRNAs (miRNAs) are non-coding RNAs with nearly 20-22-nucleotides. They modulate gene expression at the post-transcriptional level by binding to the 3′-untranslated regions (3′UTRs) of target genes or to imperfectly complementary sequences named miRNA response elements (MREs).[1] The binding of miRNAs to target genes results in the degradation or translational inhibition. Numerous human protein-coding genes are regulated by miRNAs and growing data suggest that miRNAs constitute a key part in the complex regulatory networks regulating a wide range of cellular processes, such as the timing of developmental processes, cell proliferation/differentiation, apoptosis and organ development.[2] The comprehensive studies of the past years have shown that miRNAs are not only contained into cells, but are also found outside them, released in different body fluids (e.g. serum, plasma, saliva, urine) routinely tested in patients.[3]

Although miRNA expression patterns are partially described in most cell types under normal conditions, aberrant expression of some miRNAs has been identified in various human diseases, implying that miRNAs can be beneficial as biomarkers for disease occurrence and as a possible target of treatment.[4] It has been reported that miRNA expression in tumor is up or down-regulated compared with normal tissue confirming their complex dual action either as oncogene (oncomir) or tumor suppressor gene.[5] Recently an amazing finding suggested that miRNAs are present in exosomes and these exosomal miRNAs (ex-miRNAs) can be functionally sent to target cells**.** In this minireview, we sum up latest advances in the exploration of ex-miRNAs in cancer. We also review the possible clinical utilizations of ex-miRNAs in cancer, e.g. as diagnostic markers and therapeutic targets.

Exosomes

Exosomes are small, measuring only 30–120nm in diameter, cell-derived vesicles with an endosome origin that are secreted by cells into the extracellular space. They were first discovered in the mid-1980s as small vesicles that arise from reticulocytes during their maturation to eliminate some membrane bound proteins.[6] These vesicles are generated by a various cell types such as reticulocytes, epithelial cells, neurons, and tumor cells.[7] They transfer proteins, lipids, and nucleic acids to target cells, and change the biochemical composition, signaling pathways, and gene regulation of these cells.[8] Some reports have established that exosomes are involved in immune response, tumor progression, and neurodegenerative diseases.

Exosomal miRNA and cancer

Similarly non-exosomal miRNA, ex-miRNAs have also been identified in bodily fluids.[9,10] Because of easy access and stability, ex-miRNA has been suggested as a new, minimally invasive tool for cancer diagnosis, with potential prognostic value. Ex-miRNA profiling of serum from cancer patients versus healthy individuals has shown significant differences with regard to tumor progression, highlighting a possible use of these miRs as disease prognostic biomarkers.[11] Exosomes are a reliable source of miR in bodily fluids, preventing breakdown of biological macromolecules under non-physiological conditions. It was reported that Ex-miR remains stable at -208°C for 5years and is resistant to freeze-thaw cycles.[12]

Ex-miRNA can provide an understanding for the classification or subtype of the tumour. Besides, it was found that ex-miRNAs indicate tumour severity, progression and aggressiveness. The diverse range of information that might be obtained from ex-miRNA, including progression of a tumour, identification of metastasis and possible drug resistance, could be used to affect clinical decisions and treatment strategies, thus promoting optimized treatments adjusted to meet the needs of the patient. These data could also have a prognostic value.[13] Furthermore, ex- miRNAs represent a encouraging new treatment approach due to their significant natural role in cellular processes along with high stability, tissue-specific expression and secretion into body fluids.[14]

Conclusion

Extensive effort is spent for research to ascertain new cancer diagnostic and prognostic tools. Malignant progression is significantly affected by dynamic cross-talk between stromal and cancer cells. Exosomes regulate communication between both adjacent and distant cells, thus emerging as a new form of intercellular communication, as

well as a delivery tool. As a noninvasive approach, measurement of extracellular miRNAs in bodily fluids might be a valuable strategy. Additionally, because dysregulation of miRNAs is essential to the pathogenesis of numerous cancers, they are promising candidates for clinical usage as therapeutic targets in both solid and hematological malignancies. The ex-miRNAs involved in the regulation of cancer metabolism may be possibly used for better diagnostics and treatment.

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Conflict of interest

Author declares that there is no conflict of interest.

References

1. Takahashi R, Prieto-Vila M, Hironaka A, et al. The role of extracellular vesicle microRNAs in cancer biology. *Clin Chem Lab Med*. 2017;55(5):648–656.
2. Png KJ, Halberg N, Yoshida M, et al. A microRNA regulon that mediates endothelial recruitment and metastasis by cancer cells. *Nature*. 2012;481(7380):190–194.
3. Ciesla M, Kozakowska M, Loboda A, et al. MicroRNAs as biomarkers of disease onset. *Anal Bioanal Chem*. 2011;401(7):2051–2061.
4. Iorio MV, Croce CM. MicroRNA dysregulation in cancer: diagnostics monitoring and therapeutics. A comprehensive review. *EMBO Mol Med*. 2012;4(3):143–159.
5. Lu J, Getz G, Miska EA, et al. MicroRNA expression profiles classify human cancers. *Nature*. 2005;435(7043):834–838.
6. Pan BT, Johnstone RM. Fate of the transferrin receptor during maturation of sheep reticulocytes in vitro: selective externalization of the receptor. *Cell*. 1983;33(3):967–978.
7. Théry C, Ostrowski M, Segura E. Membrane vesicles as conveyors of immune responses. *Nat Rev Immunol*. 2009;9(8):581–593.
8. Simona F, Laura S, Simona T, et al. Contribution of proteomics to understanding the role of tumor-derived exosomes in cancer progression: state of the art and new perspectives. *Proteomics*. 2013;13(1–11):1581–1594.
9. Lau C, Kim Y, Chia D, et al. Role of pancreatic cancer-derived exosomes in salivary biomarker development. *J Biol Chem*. 2013;288(37):26888–26897.
10. Saman S, Kim W, Raya M, et al. Exosome-associated tau is secreted in tauopathy models and is selectively phosphorylated in cerebrospinal fluid in early Alzheimer disease. *J Biol Chem*. 2012;287(6):3842–3849.
11. Ye SB, Li ZL, Luo DH, et al. Tumor-derived exosomes promote tumor progression and T-cell dysfunction through the regulation of enriched exosomal microRNAs in human nasopharyngeal carcinoma. *Oncotarget*. 2014;5(14):5439–5452.
12. Weber JA, Baxter DH, Zhang S, et al. The microRNA spectrum in 12 body fluids. *Clin Chem*. 2010;56:1733–1741.
13. Thind A, Wilson C. Exosomal miRNAs as cancer biomarkers and therapeutic targets. *J Extracell Vesicles*. 2016;5:31292.
14. Nouraee N, Mowla SJ. miRNA therapeutics in cardiovascular diseases: promises and problems. *Front Genet*. 2015;6:232.