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Exosomes and miRNAs: New Biomarkers?

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Introduction

Exosomes are small vesicles, between 30 nm to 100 nm in size and endosomal origin, are present in a variety of biological fluids, such as plasma, urine, saliva, semen, among others. They are produced both during and pathological conditions by a variety of cell types. However, this production by tumor cells occurs in greater abundance. These vesicles are gaining visibility in oncology studies because of their ability to act at various stages of carcinogenesis and to perform cell-cell communication by transferring their content (peptides, DNA, RNAs, miRNAs and proteins). In tumor context, they also carry oncoproteins, and immunoregulatory molecules that may contribute to cancer progression (invasion and metastasis) [1,3].

The possibility of using exosomes as a biomarker for detection, follow-up or prognosis in cancer cases has attracted a great deal of interest in these vesicles since their content reflects the secreting tissue's genomic and proteomic content. Initially, the obtaining of exosomes required sensitive techniques that, for the most part, required ultracentrifugation. However, more modern commercial kits no longer require this step, microcentrifuge with a capacity of at least 10 000xg can be used, this facilitates the analysis of these small vesicles in smaller and less resource researcher laboratories.

Because they are transport-capable vesicles and easily recognized by other cells, their therapeutic potential as a drug carrier, such as the ability to overcome through the blood-brain barrier or other molecules necessary for proper cell function, is being considered. Among the diverse possibilities of therapeutic use of the exosomes, there is the transport of microRNAs (miRNA) or anti-miRNA specific to regularize the physiological expression that was lost during the process of carcinogenesis [4].

MiRNAs are a class of small non-coding RNAs (~22nt) that act to regulate gene expression in a post-transcriptional manner. In carcinogenesis, they may act as tumor suppressors or oncogenes, depending on the target mRNA. Oncogenic miRNAs have been described in the tumorigenesis of several cancers, for example: in uterine cervix cancer, miRNAs miR-21 and miR-146a are involved in the progression of cell growth and cell invasion [5,6]. On the other hand, miR-214 and miR-218 have been described as tumor suppressors. miR-21, miR-23a, miR-203, let-7a were described in the colorectal cancer; miR-375, miR-21-5p, miR-141-5p and miR-1290 were described in prostate cancer and miR-21, miR-141, miR-203, miR-214 were described in ovarian cancer.

Some of the reasons for the interest of the use of exosomal miRNAs in oncology are the fact that they can act as tumor suppressor, interfering in the immune response, when the target is an oncogene mRNA; help in the progression of the disease, when the target is a tumor suppressor mRNA. Furthermore, it stimulates angiogenesis and development of metastasis and may also interfere in the clinical follow-up of the disease, diagnosis and prognosis of cancer [7].

Considering that miRNA concentration is different between patients and healthy people and that exosomes protects miRNA from degradation, it makes it a potential biomarker [8,9]. This opens future prospects for cancer diagnosis/prognosis and also for other diseases.

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