



## Implication of MicroRNAs in Cancer Diagnosis and Therapy

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### Editorial

MicroRNAs represent a class of small, ribonucleic acid non-coding proteins which regulates the translation rate of approximately 60% of protein coding genes, thus controlling various metabolic and cellular pathways [1]. In the mammalian genomes miRNAs are located in the intergenic regions, in the exons and introns of the non-coding genes, at the level of the introns of the protein coding genes and even in their 3'UTR region [2]. In the human genome, the miRNAs encoding regions are not randomly distributed and are located in all chromosomes except the Y chromosome [3].

MicroRNAs control protein coding genes by complementarity attaching in the cytoplasm to the messenger RNA sequence or directly by interfering with its regulatory proteins [4]. A single mRNA can be targeted by multiple miRNAs, and each miRNAs can target hundreds of genes with an average of 500 targets per miRNA [5]. miRNAs can target not only mRNA but also DNA and proteins [6]. Like mRNA, miRNAs can be transcribed in a specific manner of time and cell type [7].

The involvement of miRNAs in regulation of genes during development revealed their complex role in cancer biology. They are involved in promoting tumor growth, invasiveness, angiogenesis, and their expression is different between malignant and normal cells [8]. Amplification or deletion of genomic regions which comprise miRNA genes, abnormal transcriptional control of microRNAs and defects in their biogenesis process are mechanisms of molecular pathways perturbation involved in malignant transformation [9]. The influence of miRNAs on tumorigenesis has shown that they can act as oncogenes or tumor suppressor genes and can be classified into two categories: oncogenic miRNAs and tumor suppressive mRNAs [10].

Several miRNAs were reported to be under expressed or overexpressed in most studied cancers [11]. These aspects made possible tumors classification according to the recurrence of these expression variations [12]. Along with the intracellular role, miRNAs also have extracellular functions, being released by cells in different vesicles and being taken by receptor cells located in other parts of the body. Thus, circulating miRNAs represent a new regulatory mechanism that can influence physiological and pathological processes [13].

The approach of circulating miRNAs offers new perspectives for non-invasive cancer analyses. miRNAs have potential characteristics of reliable, non-invasive biomarkers which provide accurate diagnostic and prognostic information [14].

Their expression profiles associated with urothelial cancer are different in tumor tissue, urine and blood compared to healthy people,

suggesting that they can function by different mechanisms. Transcription of miRNAs with intragenic localization can be regulated by changes in host genes and genetic variations of binding sites may affect miRNAs functions and can have a significant impact on tumor progression [15]. For a precise and non-invasive diagnosis of urinary bladder cancer, it is necessary to add new biomarkers with increased sensitivity and specificity to current biomarkers based tests. For this, it is recommended to be targeted both selection and validation of an optimal miRNAs combination [16].

In recent years, changes in the expression of miRNAs have been explored in various types of liver diseases. Determining the expression of some miRNAs in the blood allowed the development of circulating miRNA-based model for hepatocellular carcinoma risk prediction in cirrhosis patients [17]. Plasma changes in the expression of some miRNAs in HCV infection may influence the host immune response and may be correlated with the prediction of clinical evolution [18]. In HBV chronic infections, the dynamic changes of miRNAs may help to identify the transition from chronic active hepatitis B to the inactive HBV infection in patients with sustained virological response to antiviral therapy [19].

Controlling activity of signaling molecules involved in cancer by the miRNAs, has suggested their significantly increased potential in clinical practice, as new, noninvasive diagnostic biomarkers [14]. The use of miRNAs in cancer therapy is based on selective overexpression or inhibition of a miRNAs that control important cellular processes [13]. In this context, microRNAs offer an attractive tool as biomarkers for cancer detection, diagnosis, and cancer prognosis assessment in both solid tumors and circulating tumor cells. The research and validation of these molecules will improve substantially the molecular diagnostic for personalized medicine in human cancer.

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