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The Effect of MicroRNAs on Cancer Cell

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Introduction

MicroRNAs (miRNAs) are small single-stranded noncoding RNA of about 20–25 nucleotides in length. Since finding in the early 1990s in *C. elegans* [1], these small molecules have an important role in the regulation of a wide range of biological processes, as regulation of gene expression and control many pathways as cell growth, differentiation, and apoptosis by controlling their target gene expression. The miRNAs have negative regulation of gene expression by binding 3' untranslated regions of mRNA of a protein-coding gene, producing a degradation or blockage of translation of these mRNAs [2]. One of the most recent discoveries in molecular oncology over the last decade is the interaction between abnormalities in protein-coding genes and miRNAs that are causally involved in cancer initiation, progression, and metastasis. In recent years, more data have described the active participation of miRNAs in regulating gene expression is produced by microenvironment cells [3].

Mature miRNAs reduce the stability of mRNA including; the genes mediate processes in tumorigenesis, such as cell cycle regulation, inflammation, stress response, differentiation, invasion, and apoptosis. MiRNA targeting accomplished through specific base-pairing interactions between the 5′ end of the miRNA and sites in coding and untranslated regions (UTRs) of mRNAs; target locations in the 3 UTR result in more active mRNA destabilization. From the previous studies, it became apparent that alterations in the expression of miRNA contribute to the pathogenesis of most human malignancies as; miR-15a/miR-16-1 downregulated in chronic lymphocytic lymphoma [4], miR-21 act as a potential biomarker to identify metastatic gastric cancer with chemo-resistance [5], miR-155 in colon [6], and hepatocellular carcinoma (HCC) diseases [7], miR-200 in colon cancer [8], miR-210 correlated with outcome of prostate cancer [9], miR-221 as a prognostic biomarker for the recurrence in papillary thyroid cancer [10], miR-320 was downregulated in non-small cell lung cancer [11], etc., have been found to be differentially expressed in various tumor tissues and cancer cells as (HCC), breast cancer. And accordingly their differential roles in carcinogenesis, they are categorized as either oncogenes or tumor suppressors [12].

Recently, microarray analysis has declared that a subset of miRNA are up and downregulated during the development of HCC [13]. Reductions in the expression of miRNAs acting as tumor suppressor genes are frequently observed in HCC, and the targets of these down-regulated miRNAs may be putative oncogenes. On the other hand, some of the upregulated miRNAs act as oncogenic miRNA in HCC and may be targets of tumor suppressor genes [14].

Earlier studies indicated specific changes in miRNA expression patterns in HCC as compared with normal liver tissue adjacent to tumor tissues, or liver cirrhosis which correlated with the disease outcome [15,16].

Previous studies found, the expression of 188 different miRNAs in HCC patients and adjacent normal liver tissues obtained from 12 hepatitis B virus (HBV) positive and 14 hepatitis c virus (HCV) positive patients, the expression of six miRNAs was decreased in HBV patients, and that of 13 miRNAs was decreased in HCV patients. These data suggested that there are different patterns in the miRNA profiles between HBV and HCV infection associated with HCC patients [14,17].

Earlier studies reported that miRNAs have a critical role in key pathways, which makes them useful candidates as biomarkers for cancer diagnosis and prognosis of paediatric brain tumours. In addition, their stability in bodily fluids, function in several tissues, and their capability to detect early phase disease are useful attributes [18–20]. The different treatments currently used, such as radiotherapy and chemotherapy, play an essential role in improving outcomes, but finding biomarkers for better diagnosis, prognosis, and the management of disease progression is necessary [21,22].

A previous study identified miR-29 as a negative regulator of the B7-H3 protein, which acts as a surface immunomodulatory glycoprotein inhibiting natural killer (NK) and T-cell functions [23]. A previous study showed an inverse correlation between miR-29 and B7-H3 in solid tumours in cell line experiments [24]; in addition this study showed the role of miR-29 in the promotion of anti-tumour immunity mediated by NK and T-cells [25].

Conclusion

The advancement of new sensitive detection technologies as qRT-PCR, microarray, and deep sequencing has found distinct miRNA expression profile in serum/plasma, urine, and saliva, as well as seminal, amniotic, and pleural effusions from patients with cancer. These circulating miRNAs can play an essential role in the prediction of chemotherapeutic response; in addition, their diagnostic or prognostic value [26]. So miRNAs act as promising therapeutic agents and several pharmaceutical companies already have miRNA therapeutics in their developmental pipeline [3].

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