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MicroRNAs: Promising Potential Targets for Cancer Treatment

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MicroRNAs (miRNAs) are single-stranded, non-coding RNAs, approximately 19 to 22 nucleotides in length that function as negative regulators of gene expression. MicroRNAs genes are transcribed by RNA polymerase II. The primary miRNA transcript (pri-miRNAs) is cleaved by the Drosha ribonuclease III enzyme to produce an approximately 70-nt stem-loop precursor miRNA (pre-miRNA), which is further cleaved by the cytoplasmic Dicer ribonuclease to create mature miRNA (1, 2). In the recent years, there has been heightened interest among investigators to study the role of mircoRNA (miRNA) in cancer development as well as response to treatment in cancer patients since they function as tumor suppressors or oncogenes (3, 4).

Mature miRNAs target the 3' untranslated region (3'UTR) of mRNA, leading to mRNA degradation or suppression of translation (1, 5). It has been reported that a single miRNA could bind to mRNAs of about 200 genes, therefore miRNAs play an important role in gene regulation (6, 7) and are involved in physiologic and pathologic processes (1), including tumorigenesis (8), proliferation (9) and apoptosis (10).

Single nucleotide polymorphisms (SNPs) located in miRNAs target sites and in miRNAs themselves could affect gene expression and subsequently alter individual susceptibility to cancer and may also be potential disease markers (11-14).

Growing evidence has shown that polymorphism in the miRNAs biogenesis pathway, mature miRNAs and their targets are associated with the risk of various cancers (15-30).

The aberrant miRNAs expression could serve as potential diagnostic and prognostic biomarkers to evaluate tumor initiation, progression and response to treatment in cancer patients. Down-regulation of microRNA-205 has been shown to be correlated with worse distant metastasis-free survival and overall survival of inflammatory breast cancer (31). It has been suggested that miR-26b could serve as a biomarker for inflammation-associated processes in the gastrointestinal system. As miR-26b expression is down-regulated in sporadic colon cancer, it could be used to differentiate between ulcerative colitis associated colorectal carcinoma (UCC) and the sporadic cancer type (32).

It has been reported that down-regulation of miR-26a/miR-148a and miR-148a in tumor tissues contributed to shorter overall survival of gastric cancer patients (33). A meta-analysis performed by Chen et al. (34) proposed that overexpression of miR-21 predicts both poor disease-free survival (DFS) and overall survival (OS) in patients with colorectal cancer. The results of another meta-analysis (35) showed that high expression of miRNA-21 is associated with worse OS in gliomas.

The results of meta-analysis done by Liang et al. (36) indicated that upregulation of miR-203 was not associated with OS. However, high expression of miR-203 was significantly associated with poor OS of cancer patients among Caucasians individuals. On the other hand, in Asians, a better OS association with miR-203 overexpression was determined. According to the findings, ethnicity appears to play an important role in association of miR-203 expression and cancer patient prognosis. The results of meta-analysis showed that down-regulation of miR-218 expression is significantly associated with poorer OS and DFS, and may be a new prognostic biomarker in some cancer types (37).

It has been proposed that circulating levels of miRNA-155 could serve as powerful diagnostic biomarkers for differential diagnosis of liposarcoma (38). Circulating microRNAs have been shown to be potential noninvasive biomarkers for diagnosis of osteosarcoma in Asian populations (39).

The findings of a meta-analysis suggested that de-

creased microRNAs expression might be promising markers for predicting the survival rate of cervical cancer (40). Overexpression of miR-200c might predict improved survival in females with ovarian cancer and overexpression of the miR-200 family significantly improves overall survival for Asian females (41). It has been shown that upregulation of miR-10b in patients with breast cancer was significantly associated with poor DFS (42).

In summary, dysregulation of miRNAs could serve as a potential novel therapeutic target for cancer treatment.

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