These were the most differentially expressed miRNAs, as determined by comparing biopsy expression data from patients having an early TDM versus patients with a late TDM.

In an exploration of possible associations of these miRNAs with characteristics of the tumors, the researchers found a positive association of *miR-7*, *miR-34b*, and *miR-151* with *tumor size* ($P < 0.05$), and the association of *miR-7*, *miR-210*, *miR-489*, and *miR-516−3p* with *pathological grade* ($P < 0.01$). Further analysis of the 249 genes revealed one group of miRNA (cluster 1) that was associated with good prognosis, that is, a greater value for TDM, and another group of miRNA (cluster 3) that was associated with poor prognosis, that is, a small value for TDM.

To summarize, the study found that specific miRNA sequences were differentially expressed, when comparing poor TDM patients with favorable TDM patients. Moreover, the study found that specific miRNA sequences were correlated with tumor size. Also, certain miRNA sequences were associated with pathological grade. In view of the identification of miRNAs associated with poor prognosis, the authors proposed designing drugs that could target and silence these particular miRNAs.

VI. BIOLOGY OF miRNA

miRNAs are small 19−25-nucleotide noncoding RNAs that can modulate gene expression by hybridizing to complementary target mRNAs, resulting in either inhibition of translation inhibition or in the degradation of the mRNA (23). miRNA is believed to be used for the regulation of a large proportion, perhaps 30−50%, of all human genes (24,25).

miRNAs are transcribed by RNA polymerase II or RNA polymerase III as longer primary miRNAs termed pri-miRNA (26). This molecule is subsequently cleaved into smaller segments by RNAse III. At this point, what is formed is a precursor that is about 60−70 nucleotides, which is exported to the cytoplasm and modified by another enzyme, RNAse II, to form miRNA. In turn, the miRNA is loaded onto the RNA-induced silencing complex, where it is then able to either cleave mRNA targets or to repress translation of the mRNA, dependent upon its complementarity to the target mRNA.

Regarding cancer, several miRNAs have been identified that are either proangiogenic or antiangiogenic. The antiangiogenic miRNAs include miR-221/222, which regulate the expression of the c-kit and cyclin G1 genes. The proangiogenic miRNAs include miR-126 and miR-378, which regulate expression of the *VEGF* gene. Experiments that knockout miR-126, for example, have the consequence of reducing angiogenesis.

This concerns metastasis. Detachment of cancer cells from tumors, followed by migration, invasion, and expression of enzymes that break down the extracellular matrix, are activities of cancer cells during migation and invasion in early stages of tumor progression.

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