

## 7. CIRCULATING miRNAs AS PROMISING CANCER BIOMARKERS

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**Introduction.** MicroRNAs (miRNAs) are small, non-coding RNAs (ncRNAs) of about 22 nucleotides in size that can function as potential oncogenes or tumor suppressors. Altered expression of these molecules was correlated with the occurrence of many cancer diseases and therefore they are considered a molecular tool for non-invasive cancer diagnosis and prognosis.

**Aim of study.** To highlight the role of circulating miRNAs as potential biomarkers for early cancer diagnosis and predictor of prognosis and cancer treatment.

**Methods and materials.** In order to achieve the aim of the study, various databases (miRCancer, OncomiR, miRactDB, mimiRNA, miRNAMap) were studied and a number of 31 scientific articles were analyzed.

**Results.** Aberrant expression of miRNAs in cancer is characterized by abnormal expression levels of mature or precursor miRNA transcripts in comparison with those in the corresponding normal tissues. Tumor-derived miRNAs measured in plasma can serve as non-invasive biomarkers for cancer detection. In the following, we will present some of the most conclusive examples that highlight the diagnosis potential of miRNAs. Plasma miR-21, miR-145, and miR-155 used in combination helped in distinguishing lung cancer from healthy smokers with 69.4% sensitivity and 78.3% specificity. Combination of miR-148b, miR-409-3p, and miR-801 discriminated powerfully between breast cancer cases and healthy controls. Three plasma microRNAs (miR-106b, miR-20a, and miR-221) had a statistically significant elevation in gastric cancer patients so as to serve as novel biomarkers for the early detection of the disease. Additionally, the combination of miR-16, miR-196a, and CA19-9 was more effective for pancreatic cancer diagnosis, especially in early tumor screening. Regarding the causes of the abnormal expression of circulating miRNAs in cancer, it can be mentioned that around 50% of the miRNA coding genes are located in areas of the genome that are associated with cancer, which are translocated or amplified in malignancies. Another reason is represented by the function variation of the enzymes involved in the biosynthesis of miRNA, like Drosha and Dicer 1. Consequently, a decrease in the levels of these enzymes has been reported in the case of bladder and ovarian cancers, while elevated levels are encountered in gastric and cervical squamous cell neoplasms. Lastly, the alteration of circulating miRNAs in cancer could also be caused by transcriptional errors of pri-miRNA.

**Conclusion.** Since the first discovery of circulating miRNAs, there have been a large number of studies focused on their biological functions and the potential of biomarkers in oncology. As described here, circulating miRNAs may derive from tumor cells in response to specific signals, enter the circulation in a stable form as cancer-related molecules, and contribute to early diagnosis, prognosis, and individualizing therapeutic strategies.