

Endometrial cancer is one of the most common cancers, mainly in highly developed countries of Europe and North America. Its incidence is increasing. In recent years, it has been proven that genetic mutations influence the development of endometrial cancer, which resulted in the introduction of the molecular division of EC in 2013 by The Cancer Genome Atlas (TCGA). On the other hand, the mechanisms that regulate gene expression include epigenetic mechanisms and non-coding RNAs. One type of non-coding RNA is microRNA (miR), which are not classic epigenetic factors, but play an important role in the regulation of gene expression at the post-transcriptional level.

The aim of this dissertation was to examine the relationship between the expression of three microRNAs (miR-21-5p, miR-205-5p and miR-222-3p) in endometrial cancer tissue. The objective was also to examine the stability of SNORD48 and U6 expression, which are often used as reference genes in microRNA expression studies.

The study group consisted of 111 patients with EC, whose tumor tissue was collected during hysterectomy. The control group included 19 patients undergoing surgery for uterine fibroids or pelvic organ prolapse without tumors. All patients gave written consent to participate in the study.

The dPCR method based on the use of microfluidic nanoplates and the QIAcuity dPCR system (Qiagen, Hilden, Germany) was applied to determine the absolute expression of individual microRNAs.

In endometrial cancer tissue, miR-205-5p was overexpressed, while miR-222-3p and SNORD48 expression were downregulated compared with the control group. A statistically significant correlation of miR-205-5p, U6, and SNORD48 expression with different histological grades was detected. MiR-205-5p expression grew with the increasing histopathological grade (squamous intraepithelial neoplasia - EIN = 1590, G1 = 3367.2, G2 = 8067, and G3 = 20,360), whereas U6 and SNORD expression decreased from EIN to G2 and increased again at G3 (U6: EIN = 19,032, G1 = 16,482.4, G2 = 13,642.4, G3 = 133,008; SNORD48: EIN = 97,088, G1 = 59,520, G2 = 43,544, G3 = 227,200).

The outcomes of the study show that increased expression of miR-205-5p and decreased expression of miR-222-3p and SNORD48 may affect the development of endometrial cancer. Moreover, changes in the expression of miR-205-5p, U6 and SNORD48 may be associated with the progression of endometrial cancer. The results also indicate that SNORD48 and U6, commonly used as reference genes, may affect the development and progression of endometrial cancer, and therefore should not be used for normalization.

The next stage of the study was to compare the expression level of miR-21-5p, miR-205-5p and miR-222-3p in endometrial cancer tissues with the expression level in serum. From the entire study group, 18 patients and the entire control group (n=19) were included in this stage. The expression was determined in both endometrial tissue and serum using dPCR. Statistically significant differences were observed for miR-205-5p only in tissue ($p < 0.001$) and for miR-222-3p both in tissue ($p = 0.003$) and in serum ($p = 0.019$).

Based on the conducted analyses, increased expression of miR-205-5p in endometrial cancer tissues and decreased expression of miR-222-3p in both tissues and serum were demonstrated. The results indicate that miR-205-5p and miR-222-3p may act as potential biomarkers of endometrial cancer. Of these, only miR-222-3p confirmed a significantly reduced level of expression in serum, which indicates its usefulness as an easily accessible marker in the diagnosis of this cancer. This study requires confirmation in a larger group of patients and an

increase in the number of tested microRNAs. This creates new diagnostic possibilities and, through new targeted therapies, gives us new treatment options.