miRNAs Participate in the Regulation of Oxidative Stress-Related Gene Expression in Endometrioid Endometrial Cancer

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Oxidation of DNA results in the formation of hydrolyzed DNA bases, which impairs cell growth by altering the gene expression profile and promoting the occurrence of gene mutations. In addition, damage to the DNA structure may occur, which promotes the formation of cancer. Reactive oxygen species (ROS). may therefore contribute to tumor induction and survival, as well as to treatment resistance, but their consistently high levels have a cytotoxic effect, which may be helpful in anticancer therapy. The potential relationship of ROS with microRNAs (miRNAs) is also interesting. These non-coding RNA molecules post-transcriptionally modulate gene expression and can act as oncogenes or tumor suppressors, affecting cancer development, metastasis or survival. The aim of the study was to assess the activity of genes associated with oxidative stress in endometrial cancer and to determine their relationship with miRNAs. Of the 1105 miRNAs found on the microarray, the number of miRNAs differentiating each cancer grade from the control was as follows: G1 vs. C, 131 miRNAs; G2 vs. C, 58 miRNAs; G3 vs. C, 84 miRNAs ($p < 0.05$; $FC > 2$ or $FC < -2$). The next step was to assess which of the differentiating miRNAs could participate in the regulation of the activity of PRDX2, PKD2, AQP1, SOD3, and KLF2. he obtained results indicate that overexpression of PKD2 may be related to significantly reduced activity of miR-195-3p, miR-20a and increased the levels of miR-106a, miR-328 in the early stages of endometrial cancer. At a later stage, the involvement of miR-134 is also possible. Interestingly, miR-183 initially shows a decrease in activity, which changes dramatically in G3 cancer. The reduced expression of SOD3 may be due to the increased activity of miR-328 in G1 cancer and miR-363 in G3 cancer. In the case of KLF2, miR-195-3p level was reduced while miR-363 was overexpressed. PRDX2 and AQP1 expression is most likely not regulated by miRNAs selected in microarray analysis with our criteria. A high level of PKD2 may be the result of a decrease in the activity of miR-195-3p, miR-20a, miR-134. A SOD3 level

reduction can be caused by miR-328, miR-363. In addition, miR-363 can also regulate KLF2 expression. In the course of endometrial cancer, the phenomenon of oxidative stress is observed, the regulation of which may be influenced by miRNAs.

Keywords: endometrial cancer, microRNA, microarray, oxidative stress phenomenon, molecular marker