ABSTRACT

Lung cancer is one of the most common malignancies in the world and still has the highest mortality rate. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung malignancies. The vast majority of primary lung cancers are diagnosed at a late stage of the disease, in which radical surgical treatment is not possible. The only effective treatment is chemotherapy or radiotherapy. The introduction of new methods of treatment, the so-called targeted therapies aiming molecular targets required a precise definition of the NSCLC subtype. These therapies bring the greatest therapeutic benefit in non-squamous carcinomas. With a small amount of diagnostic material, it is not always possible to clearly establish the histopathological diagnosis using histological methods. This prompts a continuous search for molecular biomarkers that precisely differentiate squamous and adenocarcinoma of the lung. Six genes (*MIR205HG, KRT5, KRT6A, PPKNEFD, SERPINB5 and DSG3*) were selected from the 53-gene differentiating signature of squamous and adenocarcinomas of the lung, the expression of which was examined in this study.

The aim of the study was to analyze the expression of selected genes at the mRNA level in primary tumors in patients in the early stages of NSCLC, to analyze the relationship between the expression level and clinicopathological parameters, to evaluate the importance of the expression levels of selected genes differentiating squamous and adenocarcinoma of the lung, and to attempt to develop a molecular test differentiating NSCLC subtypes with the assessment of its diagnostic usefulness.

The study included 140 NSCLC patients in the stage of TNM I - IIIA. The materials for molecular tests were tumor specimens collected during surgery. In each section, the expression of selected genes on the mRNA level was assessed using the Real-Time PCR technique.

Analysis of the expression of selected genes showed statistically significant differences between adenocarcinoma (ADC) and squamous cell carcinoma of the lung (SqCC). These differences were independent of the clinicopathological data. All the analyzed genes in the SqCC group showed a statistically significantly higher level of expression than in the ADC group. Using the decision tree model, the diagnostic value of the analyzed variables was determined in terms of the differentiation of histological subtypes of lung cancer into ADC and SqCC. The obtained results showed that the only classifying variable is the expression of the

DSG3 gene. The diagnostic usefulness of the tested model was assessed by plotting the ROC curve, which indicated the clinical usefulness of the analyzed predictor. The sensitivity of the developed diagnostic model was 100% and the specificity was 70.8%.

The conducted studies showed that the levels of relative expression of the analyzed genes in lung tumors did not correlate with clinicopathological factors, such as: age, sex, TNM classification stage and tumor relapse status after surgery. DSG3 may be a new, promising biomarker useful in the differential diagnosis of histological subtypes of lung cancer.

The level of expression of the *MIR205HG, KRT5, KRT6A, PPKNEFD, SERPINB5 and DSG3* genes may serve as an additional diagnostic tool for the differentiation of squamous and adenocarcinoma of the lung in terms of qualifying patients for personalized therapy.