

9. ABSTRACT

Lung cancer is one of the most common, but also the most deadly cancers, both globally and in Poland. Genetic heterogeneity of lung cancer cells may determine the course of the disease and the outcome of treatment. For this reason, new, better than the current prognostic and predictive factors for this cancer are being searched, e.g. within changes in the sequence or expression of genes. It seems particularly valuable to find markers that could be assessed in readily available biological material like peripheral blood.

The aim of the doctoral thesis was to assess the prognostic value of the *HMGA1* gene in lung cancer. This gene encodes the non-histone protein HMGA1, whose function is to regulate the transcription of other genes. Both the expression of the *HMGA1* gene and the amount of the HMGA1 protein are often elevated in cancer cells and correlate with the severity of the disease. So far, the prognostic value of the level of *HMGA1* gene expression has been demonstrated in the case of e.g. pancreatic, stomach and endometrial cancer. However, little is known about its role in lung cancer.

The conducted analyzes showed that the level of *HMGA1* expression is significantly higher in lung cancer tissue, regardless of its histological type, and may be potentially useful as a marker of neoplastic tissue. It is also related to sex, age and clinical stage of patients with lung cancer. High levels of *HMGA1* expression are associated with shorter overall and progression-free survival in patients with lung adenocarcinoma, but such a relationship has not been confirmed in patients with squamous cell carcinoma. The participation of the HMGA1 protein in the process of carcinogenesis may be associated with its functional interaction with proteins important for the regulation of the cell cycle, regulating transcription, modeling chromatin, or synthesis of cholesterol.

It was observed that the level of *HMGA1* expression in the peripheral blood of NSCLC patients monitored at the time of diagnosis, 100 days and 1 year after surgery decreased systematically over time. The level of *HMGA1* expression in the blood one year after surgery was significantly higher in smokers. There was also a trend of shorter overall survival in NSCLC patients who had high levels of *HMGA1* expression measured in blood 100 days after surgery. The conducted research allows for the conclusion that the *HMGA1* gene is an important factor involved in the process of carcinogenesis in the lung tissue, and the determination the

level of its expression both in the neoplastic tissue and in the peripheral blood has a prognostic value in patients with NSCLC.