Summary

Lung cancer is still a current clinical problem with a low five-year survival rate and little progress in treatment outcomes. In recent years, the development and introduction of new technologies has made it possible to better understand some of the molecular disorders involved in the pathogenesis of non-small cell lung cancer. Abnormal activation of the WNT/β-catenin pathway is involved in tumor proliferation, relapse, renewal of cancer stem cells, and the acquisition of resistance to anti-cancer therapies. The knowledge about the WNT/β-catenin pathway in non-small cell lung cancer is still insufficient to allow its use in diagnosis or therapy.

The aim of this study was to evaluate the mRNA expression of genes encoding WNT-4, WNT-5A, WNT-7A, WNT-11 and WNT-16 ligands involved in the activation of the non-canonical WNT/β-catenin pathways in cancer cell lines and in 80 resected tumors in early stages of non-small cell lung cancer. Additionally, the relationship between the expression of the studied ligands and the clinical and pathological features of the operated patients was assessed. The study was approved by the Bioethics Committee of the Medical University of Bialystok no: R-I-002/447/2015. All patients gave written informed consent to participate in the study. Quantification of ligand expression was performed by real-time PCR using TaqMan probes.

The expression of genes encoding ligands of the non-canonical WNT/β-catenin pathways were active, with the exception of the WNT-16 ligand, both in non-small cell lung cancer cell lines and in operated tumors. Lung cancer cell lines demonstrates the downregulation of non-canonical WNT/β-catenin ligands expression with the exception of WNT-11 which were upregulated in adenocarcinoma and WNT-5A in adenocarcinoma nad suqmous cell carcinoma cell lines. Downregulation of ligands has been demonstrated in all histopathological types of non-small cell lung cancer. In comparisons between histopathological types, overexpression of the WNT-5A ligand at the mRNA level was found in squamous cell carcinoma compared to large cell carcinoma, and WNT-7A ligand in squamous cell carcinoma compared to lung adenocarcinoma. There was no correlation between the expression of ligands at the mRNA level activating the non-canonical WNT/β-catenin pathways and the clinical and pathological features of the patients. The expression of WNT-16 ligand in lung cancer cell lines and operated tumors was undetectable.

The results of the conducted study and their comparison to available literature data suggest that ligands activating the non-canonical WNT/β-catenin pathways play a complex role in the development of non-small cell lung cancer.