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Tytuł: „Wpływ wybranych mikroRNA na agresywny fenotyp i chemiooporność komórek płaskonabłonkowego raka płuca”
Tytuł w języku angielskim: „Influence of chosen microRNAs on the aggressive phenotype and chemoresistance of lung squamous cell carcinoma”
Promotor: Dr hab. Anna Żaczek
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Obszar wiedzy: Nauki Przyrodnicze
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Abstract

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related deaths worldwide. This is mainly due to late detection and relatively low effectiveness of chemotherapy. In addition to search for new therapeutic approaches, it is also important to develop predictive and prognostic biomarkers for better stratification of patients for adjuvant treatment. Previous studies have shown that the overexpression of three microRNAs (miRNAs): miR-192-5p, miR-192-3p and miR-662-5p in patients with stage I-IIIA squamous lung carcinoma (SCC) correlated with a high risk of developing distant metastases. However, the biological role of these miRNAs in maintanence of chemoresistance and/or aggressive phenotype in SCC has not been described yet and its assessment is the research goal of this dissertation.

The expression of miR-192-5p, miR-192-3p and miR-662-5p was analyzed by RT-qPCR in a panel of NSCLC cell lines. Of these, two SCC cell lines, i.e. H520 and H1703, were used for functional analysis of the aforementioned miRNAs. Cells were transfected with miRNA inhibitors in the presence of a reporter vector, and the effect of miRNA silencing on the chemoresistance against cisplatin and etoposide, migration and clonogenicity was analyzed. Transcriptomic analysis by RNA-Seq was also performed to investigate changes that occur at the RNA level after miR-192-5p and miR-662-5p silencing.

It was shown that inhibition of miR-192-5p and miR-662-5p sensitizes H520 and H1703 cells to etoposide, but not to cisplatin. Treatment of H520 and H1703 cells with miR-192-5p and miR-662-5p inhibitors also decreased their migration ability and clonogenic potential. Downregulation of miR-192-3p did not cause any biological effect in any of the tests performed. RNA-Seq analysis allowed identification of genes potentially responsible for maintaining chemoresistance and aggressiveness, as well as those responsible for immune evasion.

These results indicate the contribution of miR-192-5p and miR-662-5p in the biology of SCC, linking chemoresistance with invasiveness. Overexpression of these miRNAs can also potentially serve as potential marker of resistance to etoposide.