ANALYSIS OF RARβ PROMOTER METHYLATION AS AN EPIGENETIC MECHANISM OF GENE SILENCING IN NON-SMALL CELL LUNG CANCER (NSCLC)

A.Dutkowska[1], A.Antczak[1], D.Pastuszak-Lewandoska[2], M.Migdalska-Sęk[2], K.Czarnecka[2], P.Górski[3], J.Kordiak[4], E.Nawrot[2] and E.Brzeziańska[2]

[1]Department of General and Oncological Pulmonology, Medical University of Lodz

[2]Department of Molecular Bases of Medicine, Medical University of Lodz

[3]Department of Pneumonology and Allergy, 1st Chair of Internal Diseases, Medical University of Lodz

[4]Department of Chest Surgery, General and Oncological Surgery University Hospital No. 2, Medical University of Lodz

Introduction: RARß gene is one of the tumor suppressor genes (TSGs), which is frequently deleted or epigenetically silenced at an early stage of tumor progression.

Material and methods: With methylation-specific PCR (MSP) and real-time-polymerase chain reaction (qPCR) techniques, we investigated the promoter methylation and expression status of RARß gene in 60 surgically resected NSCLCs and 60 corresponding unchanged tissue samples. We correlated the results with the pathological features of tumors and clinical features of patients.

Results: qPCR analysis detected statistically significant lower RARß expression in patients with adenocarcinoma (AC) and large cell carcinoma (LCC) than in patients with squamous cell carcinoma (SCC) (AC vs SCC, P=0.032; AC and LCC vs SCC, P=0.013). Additionally, significantly lower expression of RARß gene was revealed in NSCC (non-squamous cell cancer) patients with history of smoking assessed as PYs (PY<40 vs PY≥40, P=0.045).

Regarding RARß promoter methylation, we found statistically significant differences between methylation index (MI) values in SCC group when considering pTNM staging, with higher values in T1a+T1b compared with T2a+T2b and T3+T4 groups (P=0.024).

Conclusions: These findings suggest that different expression status of the RARß gene in SCC and NSCC makes the RARß gene a valuable diagnostic marker for differentiating the NSCLC subtypes.

In our study we didn’t observe any correlations between methylation status and expression level of RARß gene. It possibly suggests that another molecular mechanisms (genetic/epigenetic, e.g. ncRNA) influence RARß expression in NSCLC patients.