CHANGES IN THE LEVEL OF EXPRESSION AND PROMOTER METHYLATION OF FHIT GENE IN THE NSCLC SPECIMENS- THE SEARCH FOR NEW DIAGNOSTIC MARKERS

Karolina H. Czarnecka[1], Dorota Pastuszak-Lewandoska[1], Monika Migdalska-Sęk[1], Adam Antczak[2], Ewa Nawrot[1], Justyna Kiszałkiewicz[1], Daria Domańska[1], Jacek Kordiak[3], Paweł Górski[4], Ewa Brzeziańska[1]

karolina.czarnecka@umed.lodz.pl

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

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

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

[4] Department of Pneumology and Allergology, Medical University of Lodz

Department of Molecular Bases of Medicine

I Chair of Internal Medicine, Medical University of Lodz

92-213 Lodz, Pomorska 251 street (buiding C-5)

Introduction: Promoter hypermethylation of TSGs is an epigenetic mechanism of functional gene silencing in many types of cancers. *FHIT* promoter region hypermethylation was observed in NSCLC. Epigenetic silencing of *FHIT* can predict NSCLC outcome.

Material and method: Lung tissue specimens obtained from patients (n=61) with diagnosed NSCLC (SCC=34, AC=22, LCC=5). Matching macroscopically unchanged tissue served as control. The relative expression analysis of *FHIT:* qPCR analysis with TLDA arrays. *FHIT* promoter methylation assessment: MS-PCR, methylation index value (MI) evaluation.

Results: Statistically significant differences in mean RQ values between studied histopathological groups were observed ($p<0.05$). *FHIT* expression was higher in AC group (2.568), compared to LCC (1.808) and SCC (1.398). There were observed correlations: positive of RQ values with increased tumour sizes (TNM classification) and negative with patient's age (<60, 60-70, >70 years), however not statistically significant. *FHIT* expression was statistically significantly higher ($p<0.05$) among women (1.984) *vs.* man (1.723).

Methylated alleles of *FHIT* were observed both in NSCLC and control specimens. The mean MI value was higher in control tissue (0.472) *vs.* neoplasm (0.382). Higher levels of MI were observed in man (0.416) *vs.* women (0.343) MI value were increasing with the patient's age (years): <60 (0.296), 60-70 (0.407), >70 (0.436). There were no significant correlations between MI and RQ values.

Conclusions: Statistically significant differences in the *FHIT* expression between AC, LCC and SCC indicate gene usefulness as a diagnostic marker for NSCLC subtypes. *FHIT* epigenetic alteration both in cancer and control tissue may be important in early stage of NSCLC development.