CXCR4 AND IL-1B GENE EXPRESSION IN LUNG ADENOCARCINOMA CYTOLOGY

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Objective:

Increased values of chemokine receptor CXCR4 and interleukin-1 beta (IL-1β) gene expression are associated with distant metastases and poor outcomes in patients with various types of advanced tumors including non-small cell lung cancer. The study's aim was to analyze the CXCR4 and IL-1β gene expression in lung adenocarcinoma (LA) cytological smears depending on the presence and type of epidermal growth factor receptor (EGFR) gene mutations.

Methods:

This prospective study included 102 LA cytological smears prepared from bronchoscopic samples and stained with the May-Grünwald Giemsa in the Division of Pulmonary Cytology at University Hospital Centre Zagreb over three years. The selected LA cytological smears were divided into two numerically equal groups based on the presence or absence of EGFR gene mutations. Furthermore, EGFR gene mutations were divided into classical (ex19del; L858R) and rare (G719X; ex20ins; S768I; T790M and ex21). The RNA was extracted from all LA cytological smears. After the reverse transcription process, the CXCR4 and IL-1β gene expression was analyzed by real-time quantitative polymerase chain reaction method (RT-qPCR). The differences in CXCR4 and IL-1β gene expression between groups were tested using the Mann-Whitney test. The significance was set at $p<0.05$.

Result:

The CXCR4 and IL-1β expression were analyzed in RNA samples of 51 EGFR positive and 51 EGFR negative LA cytological smears. In the group of LA cytological smears with EGFR gene mutations the CXCR4 and IL-1β gene expression was significantly lower compared to the group without EGFR gene mutations ($p<0,05$). The expression of IL-1β gene was 9,029 times lower in LA cytological smears with EGFR gene mutations than in samples without the mutations, while the expression of CXCR4 gene was 19,085 times lower in LA cytological smears with EGFR gene mutations than in samples without

the mutations. Classical EGFR gene mutations were detected in 34 (66.7%) LA cytological smears and rare mutations in 11 (21.6%) smears. Six (11.7%) LA cytological smears had a combination of classical and rare EGFR gene mutations. There was no significant association between CXCR4 and IL-1β gene expression when different types of EGFR gene mutations were observed.

Conclusion:

Significant differences in CXCR4 and IL-1β gene expressions between lung adenocarcinoma with EGFR gene mutations and lung adenocarcinoma without EGFR gene mutations in cytological smears were observed. The obtained results indicate the need for further research into the role of CXCR4 and IL-1β as potential predictive or prognostic molecular biomarkers.