The Correlation Between AEG-1 Expression and Radio-sensitivity and Prognosis in Non-small Cell Lung Cancer

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BACKGROUND: Astrocyte elevated gene-1 (AEG-1) has been proved to play multiple important roles in oncogenesis and cancer progression. However, the correlation between AEG-1 expression and radiotherapy in non-small cell lung cancer (NSCLC) remain unclear. Our study aims to analysis the association between AEG-1 expression level and NSCLC, particularly the relationship with radio-sensitivity and prognosis of NSCLC patients.

HYPOTHESIS: The AEG-1 expression will be widely detected in both NSCLC cell lines and patients. AEG-1 plays important roles in NSCLC proliferation, migration, invasion and apoptosis. Knockdown of AEG-1 may enhance the radio-sensitivity of NSCLC. Patients with AEG-1 high expression incline to have more severe disease. The AEG-1 high expression indicate worse OS、DFS and LRFS in NSCLC patients. Patients with low AEG-1 expression may receive the greatest benefit from postoperative radiotherapy. AEG-1 may be an attractive therapeutic target for NSCLC.

METHODS: The expression levels of AEG-1 mRNA and DNA-PKcs mRNA in A549 and H520 were evaluated by qRT-PCR. Protein expressions in lung cancer cell lines were detected using Western Blot assay. Knockdown of AEG-1 was conducted by siRNA. The cell vitality was analyzed by CCK-8 Kit. Cell migration and invasion ability was analyzed by Transwell assay. Cell apoptosis and the distribution of cell cycle were detected using Flow cytometry. The radio-sensitivity of cell lines were measured by a clonogenic assay. The AEG-1 expression was analyzed by immunohistochemistry in 225 primary NSCLC specimens and 42 adjacent normal lung tissue specimens.

RESULTS: The expression of AEG-1 was significantly higher in NSCLC tissues compared with adjacent normal lung tissues and associated with the pathologic stage ($P<0.001$) and lymph node status ($P=0.028$). The AEG-1 expression was negatively correlated with overall survival (OS) ($P=0.003$) and disease-free survival (DFS) ($P<0.001$). In postoperative radiotherapy group, the local recurrence-free survival (LRFS) was significantly shorter in patients showed high AEG-1 expression ($P=0.016$). Both univariate and multivariate analysis indicated AEG-1 expression was an independent prognostic factor for OS and DFS. In vitro, knockdown of AEG-1 expression decreased cell vitality and inhibited cell migration and invasion. Moreover, knockdown of AEG-1 expression increased cell apoptosis inducing by radiation and reduced the proportion of S phrase in cell cycle in A549 cell line. Knockdown of AEG-1 expression reduced the expression of DNA-PKcs significantly. Knockdown of AEG-1 expression enhance the radio-sensitivity of A549 cell line.