Change of the EGFR expression and downstream signal pathway in A549 cell treated with ZD1839

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Object: Discuss the change of the EGFR expression and downstream signal pathway in A549 cell treated with ZD1839.

Methods: The inhibition of the A549 cell treated with ZD1839 was measured by MTT assay and Real-Time PCR was used to evaluate the expression of EGFR and downstream signal pathway.

Results: A549 cell was inhibited by ZD1839 in vitro. After treated with ZD1839, the expression of EGFR was 1.10 fold compared with the cell without ZD1839 and Ras gene was 1.09 fold. The expression of MAPK was 52.1 percent of the cell without ZD1839, PI3K was 16.4 percent and Akt was 25.3 percent. ZD1839 didn’t affect the expression of EGFR and Ras in A549 cell but down regulated the expression of MAPK, PI3K and Akt.

Conclusion: ZD1839 inhibited A549 cell by inhibiting the tyrosine kinase activity of EGFR and the PI3K/Akt, MAPK signal pathway.

Expression and significance of RUNX3 in human lung cancer

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Background: Lung cancer is the leading cause of cancer related deaths throughout the world. A better understanding of the molecular pathogeneses of lung cancers is needed in order to achieve a preventive or therapeutic breakthrough for reducing the number of deaths. Runx-related transcription factor 3 (RUNX3) has recently been shown to be down-regulated in human cancer tissues, including lung cancer. However, the clinical value of that finding is largely unknown. We investigated the associations of RUNX3 expression in lung cancer tissues with clinical characteristics and tumor recurrence.

Materials and Methods: The expression of RUNX3 in lung cancer cell lines was examined using a quantitative real-time reverse transcriptase-polymerase chain reaction (RT-PCR) method. We also determined whether the expression of RUNX3 in the cell lines was associated with hemizygous deletion of the locus and methylation status in the exon 1. Further, we investigated the methylation status of RUNX3 using a methylation specific PCR (MSP) technique and studied hemizygous deletion using biocolor fluorescence in situ hybridization (FISH). In addition, primary lung tissues were obtained from Kyoto Prefectural University of Medicine, Japan. Among the 56 cases confirmed as primary lung carcinomas, 40 were adenocarcinomas, 15 were squamous cell carcinomas, and 1 case was large cell carcinoma. The intratumoral expression level of RUNX3 mRNA was determined and compared with that in adjacent non-tumorous lung tissue using quantitative real-time RT-PCR in the 56 cases of non-small cell lung cancer. From those results, the relationship between the expression level of RUNX3 and clinicopathological factors was examined.

Results: RUNX3 gene expression was reduced or disappeared in all cell lines examined (P < 0.001). Eight of 15 lung cancer cell lines revealed methylated bands of RUNX3, whereas 7 showed unmethylated bands. Further, hemizygous deletion of RUNX3 was observed in 8 of the cell lines by biocolor FISH. RUNX3/GAPDH mRNA levels were significantly different between tumor tissues from the lung cancer specimens and adjacent non-malignant lung tissues (P < 0.001). No significant differences in RUNX3/GAPDH mRNA levels were found related to age, gender, lymph node metastasis or tumor recurrence in the non-small cell lung cancer cases.

Conclusions: The present clinical and experimental data suggest that the comprehensive study of RUNX3 using quantitative real-time RT-PCR, MSP, and FISH would be beneficial for understanding the pathogenetic mechanisms of human lung cancer at the molecular level.

Identification of novel tumor suppressor gene candidates in small cell lung cancer for use in cancer gene therapy

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Small cell lung cancer (SCLC) is a deadly disease with no current satisfactory treatments. There is thus an urgent need for development of more efficient treatment modalities for patients with this cancer form. One intriguing modality is cancer gene therapy and one the most common approaches is tumor suppressor restoration therapy. In tumor suppressor restoration therapy a wild-type tumor suppressor gene (TSG) is