

## Upregulation of the Chemokine Receptor CCR7 expression by HIF-1 $\alpha$ and HIF-2 $\alpha$ in non-small cell lung cancer

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### 摘要

Background and objective CCR7 is closely related with the lymph node metastasis of non-small cell lung cancer. The objective of this work is to investigate the expressions of chemokine receptor CCR7, hypoxia inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ) and hypoxia inducible factor 2 $\alpha$  (HIF-2 $\alpha$ ) protein in non small cell lung cancer and the relationships of their expression, and to study the mechanism of CCR7 upregulation in NSCLC. Methods The levels of expressions of CCR7, HIF-1 $\alpha$  and HIF-2 $\alpha$  protein were detected in 94 specimens of human primary non small cell lung cancer by immunohistochemical S-P method. Human lung adenocarcinoma cell line A549 cells were transfected by lipofection with HIF-1 $\alpha$  siRNA/HIF-2 $\alpha$  siRNA, the change of CCR7 was observed by RT-PCR and immunofluorescence staining. Correlations between the expression of CCR7 and HIF-1 $\alpha$ , HIF-2 $\alpha$  were respectively analyzed. Results Immunohistochemistry showed that CCR7 was distributed in cytoplasm and/or membrane of tumor cells, HIF-1 $\alpha$ , HIF-2 $\alpha$  was distributed in nucleus and/or cytoplasm of tumor cells. The levels of expressions of CCR7, HIF-1 $\alpha$  and HIF-2 $\alpha$  protein were found to be 75.53% (71/94), 54.25% (51/94) and 70.21% (66/94) in non small cell lung cancer, respectively. the levels of expression of CCR7 protein were closely related to the clinical stages ( $P < 0.001$ ) and lymph node metastasis ( $P < 0.001$ ) of non small cell lung cancer, but there was no correlation with age, gender, histology ( $P > 0.05$ ). Furthermore, A significant correlation were found among CCR7, Hif-1 $\alpha$  and HIF-2 $\alpha$  ( $r = 0.272$ ,  $P < 0.01$ ) ( $r = 0.225$ ,  $P < 0.05$ ). In addition, the expression of CCR7 mRNA and protein levels were decreased in the transfected specific HIF-1 $\alpha$ , HIF-2 $\alpha$ siRNA group ( $P < 0.05$ ). Conclusion CCR7 expression is significantly associated with non small cell lung cancer invasion and metastasis. The upregulation of CCR7 is regulated by HIF-1 $\alpha$  and HIF-2 $\alpha$  in non small cell lung cancer.






### 关键词

CCR7; HIF-1  $\alpha$ ; HIF-2  $\alpha$ ; Lung neoplasms


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


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