

## siRNA 沉默HIF-1 $\alpha$ 在缺氧状态下对食管鳞癌细胞VEGF表达的影响

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### Effect of Silencing HIF-1 $\alpha$ by siRNA on Expression of Vascular Endothelial Growth Factor in Carcinoma Cell under Hypoxia

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- 摘要
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**摘要** 目的 观察体外乏氧培养条件下食管鳞癌细胞系EC9706中HIF-1 $\alpha$ 和VEGF的表达,探讨HIF-1 $\alpha$ 在低氧条件下对食管鳞癌细胞VEGF表达的调控作用。方法 CoCl<sub>2</sub>化学缺氧法模拟肿瘤缺氧环境,RT-PCR、免疫组化法和免疫印迹法分别检测缺氧状态下HIF-1 $\alpha$ 在mRNA和蛋白水平的表达。采用化学合成小干扰RNA (siRNA) 介导的RNA干扰技术 (RNAi) 用siRNA转染EC9706细胞,观察转染后HIF-1 $\alpha$ 沉默效果。结果 低氧条件下,EC9706细胞HIF-1 $\alpha$ mRNA水平稳定,蛋白表达显著升高,而VEGFmRNA和蛋白表达显著升高。siRNA转染EC9706后能够显著下调HIF-1 $\alpha$ 的基因表达,同时VEGF基因的表达也受到明显抑制。结论 缺氧促使食管鳞癌细胞HIF-1 $\alpha$ 在蛋白水平表达升高,并通过转录激活VEGF的机制调控食管鳞癌血管生成。

**关键词:** 食管鳞癌 乏氧诱导因子-1 $\alpha$  血管内皮生长因子 双链RNA RNA 干扰

**Abstract:** Objective To investigate the expression of HIF-1 and vascular endothelial growth factor (VEGF) in human esophageal squamous cell carcinoma cell line EC9706 under hypoxia. To observe the effect of HIF-1 $\alpha$  on hypoxia-induced VEGF expression and angiogenesis regulation pathway in esophageal squamous cell carcinoma. Methods CoCl<sub>2</sub> was used as a chemical hypoxia-inducible reagent to mimic tumor hypoxic microenvironment. mRNA and protein levels of HIF-1 $\alpha$  and VEGF were detected by semiquantitative reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemistry. With RNA interference (RNAi) originated by small interference RNA (siRNA) to use siRNA transfected EC9706 cells. Western-blot was used to observe the gene silencing effect on HIF-1 $\alpha$ . RT-PCR and immunohistochemistry were used to observe the change of VEGF gene expression after HIF-1 $\alpha$  gene silence. Results Under hypoxia, mRNA level of HIF-1 $\alpha$  was stable, while its protein level increased significantly. Both mRNA and protein levels of VEGF were up-regulated. The siRNA targeting HIF-1 $\alpha$  gene down-regulated HIF-1 $\alpha$  gene expression in cells efficiently, and VEGF gene was down-regulated as well. Conclusion Hypoxia can increase protein level of HIF-1 $\alpha$  in esophagus. HIF-1 $\alpha$  up-regulates the gene expression of VEGF which promotes angiogenesis in esophagus under hypoxic microenvironment.

**Key words:** Esophageal squamous cell carcinoma Hypoxia-inducible factor-1 alpha Vascular endothelial growth factor Double stranded RNA RNA interference

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