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低氧诱导因子HIF-1  $\alpha$  调控CX3CR1 在胰腺癌细胞中的表达\*

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Regulation of CX3CR1 expression in pancreatic cancer cells by hypoxia inducible factor 1 $\alpha$ 

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摘要

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**摘要** 目的: 以胰腺癌细胞株Patu 8988为研究对象, 通过过表达和干扰低氧诱导因子 (HIF-1  $\alpha$ ), 观察CX3CR1 表达水平的变化, 并探讨CX3CR1 在胰腺癌中的调控机制。方法: 分别构建pcDNA 3.1-HIF-1  $\alpha$  过表达质粒和HIF-1  $\alpha$ -siRNA, 转染胰腺癌细胞株Patu 8988, 经Western blot、半定量PCR 检测CX3CR1 的表达情况。采用染色质免疫沉淀 (chromatin immunoprecipitation, ChIP)、荧光素酶技术探查HIF-1  $\alpha$  与CX3CR1 启动子区的结合情况。结果: Patu 8988转染pcDNA 3.1-HIF-1  $\alpha$  后CX3CR1 的表达增加, 敲除HIF-1  $\alpha$  后CX3CR1 的表达减少。HIF-1  $\alpha$  与CX3CR1 启动子区的低氧反应元件直接结合, 并上调CX3CR1 启动子的活性 ( $P < 0.01$ )。结论: HIF-1 $\alpha$ 调控CX3CR1 在胰腺癌细胞中的表达。

**关键词**: HIF-1 $\alpha$ , CX3CR1, 胰腺癌

**Abstract**: Objective: This study aimed to investigate the effect of hypoxia inducible factor 1  $\alpha$  (HIF-1  $\alpha$ ) expression on CX3CR1 and its regulatory mechanism in pancreatic cancer cell line Patu 8988. Methods: The highly expressed plasmid pcDNA3.1 HIF-1  $\alpha$  and siRNA HIF-1  $\alpha$  were initially constructed. After the plasmid was separately transfected to the pancreatic cancer cells, CX3CR1 and HIF-1  $\alpha$  expressions were assayed by western blot analysis and real-time quantitative reverse transcriptase-polymerase chain reaction. The relationship between HIF-1  $\alpha$  and CX3CR1 promoter was determined by chromatin immunoprecipitation and luciferase technology. Results: The overexpressed HIF-1  $\alpha$  could upregulate the CX3CR1 expression in pancreatic cancer cells. The CX3CR1 expression was significantly reduced when HIF-1  $\alpha$  was knocked down. Chromatin immunoprecipitation assay demonstrated that HIF-1  $\alpha$  could be directly bound to the hypoxia-response element (5'-A/GCGTG-3') of the CX3CR1 promoter. This binding activity was significantly enhanced under hypoxic condition. CX3CR1 promoter-induced HIF-1 $\alpha$  overexpression could significantly upregulate the expression of luciferase reporter genes in pancreatic cancer cells ( $P < 0.01$ ). Conclusion: HIF-1  $\alpha$  could regulate CX3CR1 expression in pancreatic cancer cells.

**Key words**: hypoxia inducible factor 1 $\alpha$ , CX3CR1, pancreatic cancer

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