

Notch1信号途径在食管鳞癌细胞中的激活及对细胞周期的影响

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Activation of Notch1 Signaling Pathway in Esophageal Squamous Cell Carcinoma

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摘要 目的 观察Notch1信号途径在食管鳞癌EC9706细胞中的激活状态及其对细胞周期的影响。方法 通过免疫细胞化学方法检测Notch1基因在食管鳞癌细胞株EC9706细胞中的表达,并通过免疫荧光方法研究Notch1基因在EC9706细胞中的激活状态。结果 转染pcNICD后的食管鳞癌细胞株中发现Notch1基因的表达。免疫显示,转染pcNICD后的食管鳞癌细胞株中Notch1信号途径处于激活状态。与未处理和转染pcDNA3.1的EC9706细胞相比,转染pcNICD的EC9706细胞的生长速率明显受到抑制($P < 0.01$)。此外,与未处理的和转染pcDNA3.1的EC9706细胞相比,转染pcNICD的EC9706细胞的CDK2, cyclin D1和E基因的mRNA和蛋白的表达明显下调($P < 0.05$)。转染pcNICD的EC9706细胞在G₀/G₁期的比率高达74.5%,而未处理的和转染pcDNA3.1的EC9706细胞在G₀/G₁期的比率分别为59.1%和59.0%。分析显示瞬时表达NICD的EC9706细胞在G₀/G₁期比率的增加,提示激活的Notch1信号途径能够诱导细胞静止在G₀/G₁期。

此外,采用RT-PCR和Western blot技术检测与细胞周期相关基因的表达,最后通过流式细胞仪检测细胞周期的分布。结果 转染pcNICD后的食管鳞癌细胞株中发现Notch1基因的表达。免疫显示,转染pcNICD后的食管鳞癌细胞株中Notch1信号途径处于激活状态。与未处理和转染pcDNA3.1的EC9706细胞相比,转染pcNICD的EC9706细胞的生长速率明显受到抑制($P < 0.01$)。此外,与未处理的和转染pcDNA3.1的EC9706细胞相比,转染pcNICD的EC9706细胞的CDK2, cyclin D1和E基因的mRNA和蛋白的表达明显下调($P < 0.05$)。转染pcNICD的EC9706细胞在G₀/G₁期的比率高达74.5%,而未处理的和转染pcDNA3.1的EC9706细胞在G₀/G₁期的比率分别为59.1%和59.0%。分析显示瞬时表达NICD的EC9706细胞在G₀/G₁期比率的增加,提示激活的Notch1信号途径能够诱导细胞静止在G₀/G₁期。

Notch1信号途径的激活引起食管鳞癌细胞的细胞周期静止,提示Notch1基因有可能成为治疗食管鳞癌的新靶点。

关键词: Notch1信号途径 细胞周期 pcNICD载体 EC9706细胞

Abstract: Objective To investigate the active status of Notch1

signaling pathway in esophageal squamous cell carcinoma

(ESCC) and its effect on cell cycle. Methods The

expression of Notch1 gene was detected by

immunocytochemistry in EC9706 cells, and the active

status of Notch1 signaling pathway was investigated by

immunofluorescence. In addition, cell proliferation assay

was performed using CCK-8 Kit. Proteins and mRNA of the

genes related to cell cycle was studied by Western blot

and RT-PCR techniques. Finally, cell cycle distribution

was measured by flow cytometry (FCM). Results The

expression of Notch1 gene was found in EC9706 cells

transfected with pcNICD. Besides, the result of

immunofluorescence revealed that Notch1 appeared to be

expressed in the cytosol and nucleus, implying an

activated status. EC9706 cells had an obvious decreased

growth rate compared to the control EC9706 cells and

EC9706 cells transfected with pcDNA3.1 ($P < 0.01$).

Furthermore, the mRNA and proteins expressions of the

CDK2, cyclin D1 and cyclin E genes were significantly

decreased in the EC9706 cells transfected with pcNICD compared to those of the cells untreated and transfected with pcDNA3.1. There were higher proportions of cells (74.5%, $p < 0.05$) in EC9706 cells transfected with pcNICD at G_0/G_1 phase than that in cells untreated (59.1%) and transfected with pcDNA3.1 (59.0%). Cell cycle distribution analysis demonstrated that the cell increased ($p < 0.05$) at G_0/G_1 phase in the cells transiently expressing NICD, which suggested that active Notch1 signaling pathway induces G_0/G_1 cell cycle arrest in EC9706 cells. Conclusion Active Notch1 signaling pathway can obviously inhibit the growth of EC9706 cells, suggesting Notch1 gene may be a new target of treating esophageal squamous cell carcinoma.

Key words: Notch1 signaling pathway Cell cycle pcNICD vector EC9706 cell

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