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CAR的表达调节对肝癌基因治疗中腺病毒载体感染效率的影响　点此下载全文

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摘要：

目的: 通过抑制Raf MEK ERK信号转导途径调节肝癌细胞表面柯萨奇病毒和腺病毒受体(coxsackie adenovirus receptor,CAR)的表达,探索肝癌基因治疗中CAR表达与腺病毒(adenovirus, Ad)感染效率之间的关系。方法: 选择两株人肝癌细胞株SMMC－7721及HepG2，以Raf MEK ERK信号转导抑制剂U0126作用后,应用Western blotting检测细胞表面CAR蛋白的表达水平。选用能表达GFP的非复制型E　1A缺陷的Ad感染人肝癌细胞SMMC－7721及HepG2,应用FACS分析U0126处理前后Ad感染效率的变化。结果: 细胞经MEK抑制剂U0126处理后，细胞膜表面CAR的表达呈明显上调趋势。FACS检测显示,经U0126处理后,在相同感染复数(10 MOI)Ad GFP的感染下,GFP　+细胞率明显升高, SMMC 7721细胞由（71.65±6.21）%上升至（86.54±5.70）%；HepG　2细胞由（77.53±4.62）%上升至（87.06±2.83）%（均P<0.05)。结论: 抑制剂U0126抑制Raf MEK ERK信号转导途径后,可上调肝癌细胞膜表面CAR的表达,从而导致Ad在肝癌细胞感染效率的提高。

关键词：柯萨奇病毒和腺病毒受体 U0126 腺病毒 感染效率 肝细胞癌 基因治疗

Influence of coxsackie adenovirus receptor expression on infection efficiency of adenovirus vector in gene therapy of hepatocellular carcinoma　Download Fulltext

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Abstract:

To explore the relationship between coxsackie adenovirus receptor (CAR) expression and the infection efficiency of adenovirus vector in gene therapy for hepatocellular carcinoma through regulating CAR expression on cells surface　via　inhibition of the Raf/MEK/ERK pathway. Methods: Western blotting analysis was used to examine CAR expression in hepatocellular carcinoma cells (SMMC-7721 and HepG　2) before and after treatment with U0126, inhibitor of Raf/MEK/ERK signal transduction. SMMC-7721 and HepG　2 were infected by a non replicating, E1A deleted adenovirus expressing EGFP (Ad-GFP). FACS was used to analyze the infection efficiency of Ad before and after U0126 treatment. Results: The expression of CAR on cell surface had an increasing tendency after treatment with U0126. FACS analysis showed significantly increased infectivity of cells treated with the MEK inhibitor U0126 compared with untreated cells: SMMC-7721,（71.65±6.21）%→（86.54±5.70）%, HepG　2,（77.53±4.62）%→（87.06±2.83）%, when infected with Ad GFP at the same MOI (10 MOI). Conclusion: The inhibition of Raf/MEK/ERK pathway by U0126 may　up regulate　the expression of CAR in some hepatocellular carcinoma cells, which subsequently enhances the susceptibility of adenovirus infection to target cells.

Keywords:coxsackie adenovirus receptor U0126 adenovirus infection efficiency hepatocellular carcinoma gene therapy

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