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腺病毒E1a基因增强P16 基因诱导SMMC-7721肝癌细胞的凋亡

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胡还章 王伟国 马炬明 苏长青 江艺

南京军区福州总医院 肝胆外科，福建 福州 350025；第二军医大学 东方肝胆外科医院 病毒治疗研究室，上海 200438;南京军区117医院 消化内科，浙江 杭州 310004;南京军区117医院 消化内科，浙江 杭州 310004;第二军医大学 东方肝胆外科医院 病毒治疗研究室，上海 200438;南京军区福州总医院 肝胆外科，福建 福州 350025

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摘要：

目的：研究腺病毒 E1a基因与P16 抑癌基因协同对肝癌SMMC-7721细胞凋亡和增殖的影响，探索肿瘤基因治疗新模式。 方法： 构建 E1a 基因真核表达质粒pDC315-E1a和携带 P16 的重组病毒AdCMV-P16，RT-PCR和免疫荧光标记法检测pDC315-E1a质粒转染或AdCMV-P16病毒感染后SMMC-7721细胞中 P16和E1a 的表达。建立裸鼠SMMC-7721细胞移植瘤模型，pDC315-E1a和AdCMV-P16单独或联合治疗，观察其对移植瘤生长的抑制作用，免疫组化和TUNEL法分别检测移植瘤组织中P16、E1a蛋白的表达和移植瘤细胞的凋亡。 结果： SMMC-7721细胞感染AdCMV-P16或转染pDC315-E1a后， P16、E1a mRNA和蛋白水平均呈阳性表达。与空白对照组相比，AdCMV-P16治疗组移植瘤细胞凋亡率为（14.3±2.5）%（P<0 01），抑瘤率为36.1%（P<0.01）；pDC315-E1a治疗组抑瘤率为17.1%（P>0.05），移植瘤细胞凋亡率为（8.5±2.9）%（P<0.01）；AdCMV-P16联合pDC315-E1a治疗组移植瘤细胞凋亡率为（27.3±6.3）%（P<0.01），抑瘤率达57.2%（P<0.01）。 结论： 腺病毒 E1a 基因能够增强 P16 基因对肝癌SMMC-7721细胞移植瘤的抑制作用，促进移植瘤细胞的凋亡，增强 P16 基因治疗的效果。

关键词：肝癌 P16 基因 E1a 基因 腺病毒 凋亡

Adenovirus E1a gene enhances P16 gene-induced apoptosis of hepatocellular carcinoma SMMC-7721 cells

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HU Huan-zhang WANG Wei-guo MA Ju-ming SU Chang-qing JIANG Yi

Department of Hepatobiliary Surgery, Fuzhou General Hospital of Nanjing Military Area Command of PLA, Fuzhou 350025, Fujian, China; Institute of virus therapy, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, 200438;Department of Internal Medicine, No. 117 Hospital of Nanjing Military Area Command of PLA, 310004 Hangzhou, Zhejiang, China;Department of Internal Medicine, No. 117 Hospital of Nanjing Military Area Command of PLA, 310004 Hangzhou, Zhejiang, China;Institute of virus therapy, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, 200438;Department of Hepatobiliary Surgery, Fuzhou General Hospital of Nanjing Military Area Command of PLA, Fuzhou 350025, Fujian, China

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Abstract:

Objective :To investigate the synergistic effect of anti-cancer P16 gene and adenovirus E1a gene on apoptosis and proliferation of hepatocellular carcinoma SMMC-7721 cells, and to explore the novel therapeutic strategy for tumor gene therapy. Methods: Eukaryotic expression plasmid pDC315-E1a and adenoviral vector AdCMV-P16 were constructed. The expression of P16 and E1a in SMMC-7721 cells after pDC315-E1a transfection or AdCMV-P16 infection was determined by RT-PCR and immunofluorescent labeling. SMMC-7721 cell transplanted tumors in nude mice was established. The effect of pDC315-E1a and AdCMV-P16 alone or incombination on tumor growth was observed, and the expressions of P16 and E1a in transplanted tumor tissues and apoptosis of transplanted tumor cells were determined by immunohistochemistry and TUNEL assay, respectively. Results: SMMC-7721 cells showed positive expression of both mRNA and protein levels of E1a and P16 after pDC315-E1a transfection or AdCMV-P16 infection, respectively. Compared with the control group, the apoptosis rate of transplanted tumor cells was (14.3±2.5)% (P<0.01) and tumor inhibitory rate was 36 1% (P<0.01) in AdCMV-P16 therapy group; those in pDC315-E1a therapy group was (8.5±2.9)% (P<0.01) and 17.1% (P>0.05); and in AdCMV-P16 combined pDC315-E1a therapy group was (27.3±6.3)% (P<0.01) and 57.2% (P<0.01), respectively. Conclusion: Adenovirus E1a gene can increase P16-induced apoptosis and cell growth inhibition in SMMC-7721 cell transplanted tumors, and thus enhance the efficacy of P16 gene therapy.

Keywords:hepatocellular carcinoma P16 gene E1a gene adenovirus apoptosis

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