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pGPU6/GFP/Neo-hTERT-shRNA对结直肠癌SW480细胞裸鼠移植瘤的抑制

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摘要：

目的： 研究靶向hTERT基因的重组质粒pGPU6/GFP/Neo-hTERT-shRNA对人结直肠癌SW480细胞裸鼠移植瘤的治疗作用。 方法： 于裸鼠右侧腋下皮下注射人结直肠癌SW480细胞建立结直肠癌移植瘤动物模型，随机分为生理盐水组（NS组）、pGPU6/GFP/Neo-NC-shRNA组（NC-shRNA组）和pGPU6/GFP/Neo-hTERT-shRNA组（hTERT-shRNA组），各组连续进行相应治疗6次后，观察肿瘤的生长状况，测量肿瘤体积并绘制肿瘤生长曲线，H-E染色观察肿瘤组织形态学变化，免疫组织化学法检测移植瘤组织中hTERT蛋白的表达，TUNEL法检肿瘤组织中细胞凋亡情况，RT-PCR法检测瘤组织中hTERT mRNA的表达。 结果： 与NC-shRNA组和NS组比较，hTERT-shRNA组移植瘤体积增长速度减慢；hTERT-shRNA组移植瘤组织中见肿瘤细胞形态明显改变，凋亡细胞数明显增多\[（36.30±5.05)% vs (5.25±1.06)%、(6.95±1.07)%，P<0.01\]；hTERT-shRNA组hTERT的 mRNA 和蛋白表达均明显受到抑制（171.42±30.94 vs 146.89±21.43、137.35±25.49，P<0.01；0.39±0 09 vs 0.81±0 335、 0.750± 0.206，P<0 05）。 结论： 重组质粒pGPU6/GFP/Neo-hTERT-shRNA通过下调hTERT mRNA和蛋白水平的表达促进肿瘤细胞的凋亡，抑制结直肠癌移植瘤的生长。

关键词：RNA干扰 hTERT基因 结直肠癌 裸鼠 凋亡

Inhibition of pGPU6/GFP/Neo-hTERT-shRNA on colorectal cancer SW480 cell xenograft in nude mice

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Abstract:

Objective：To investigate the treatment effect of recombinant plasmid pGPU6/GFP/Neo-hTERT-shRNA targeting hTERT gene on human colorectal cancer SW480 cell xenograft in nude mice. Methods: Human colorectal cancer SW480 cells were subcutaneously implanted under the skin of the right armpit to establish nude mice model of colorectal cancer, after the tumors grew to a definite size. The mice were randomly divided into three groups: normal saline (NS group), pGPU6/GFP/Neo-NC-shRNA group（NC-shRNA group）and pGPU6/GFP/Neo-hTERT-shRNA group（hTERT-shRNA group）. After each group was treated for 6 consecutive times, the growth status of the tumor was observed, tumor volume was measured, tumor growth curve was drawn，tumor tissue morphology was observed with H-E staining, the expression of hTERT protein in the tumors was detected by immunohistochemistry, cell apoptosis was inspected by terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling(TUNEL), and the expression of hTERT mRNA was checked by RT-PCR. Results: The growth of tumor volume became slower in hTERT-shRNA group than did that in NS group and NC-shRNA group. Compared with NS group and NC-shRNA group, the tumor cell morphology changed obviously and the number of apoptotic cells increased significantly in the transplanted tumor tissues in hTERT-shRNA group（\[36 3±5 05\]% vs \[5.25± 1.06\]%, \[6.95±1.07\]%，P<0.01). Compared with NS group and NC-shRNA group, the expression of hTERT protein was significantly inhibited in hTERT-shRNA group（\[171.42±30.94\] vs \[146 89±21.43\], \[137 35±25.49\], P<0.01）. Compared with NS group and NC-shRNA group, the expression of hTERT mRNA was significantly inhibited in hTERT-shRNA group （0.39±0.09 vs 0.81±0.34, 0.75±0.21, P<0.05）. Conclusion: Recombinant plasmid pGPU6/GFP/Neo-hTERT-shRNA promotes apoptosis of implanted human colorectal cancer by down-regulating the expression of hTERT mRNA and hTERT protein in tumor tissues, thus inhibiting the growth.

Keywords:RNA interference hTERT gene colorectal cancer nude mice apoptosis