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受体依赖性TRAIL重组腺病毒对人肺癌细胞凋亡的诱导作用 点此下载全文

马玲娣 王 勇 倪 诚 王仕忠 鲍永仪 关乃富 张 科 Leif G. Salford 樊小龙

南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;南京医科大学 附属常州市第二人民医院 中心实验室，江苏 常州 213003;The Rausing Laboratory, Lund University, SE 22184 Lund, Sweden;The Rausing Laboratory, Lund University, SE 22184 Lund, Sweden

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摘要：

目的：观察重组TRAIL腺病毒（Ad5 TRAIL及Ad5F35 TRAIL）对人非小细胞肺癌（nonsmall cell lung cancer，NSCLC）原代培养细胞和细胞株的凋亡诱导作用，探讨两种Ad TRAIL用于肺癌基因治疗的价值。方法：采用流式细胞术检测人肺癌细胞系A549、Z793、QG56和NCI H520及10例原代培养肺癌细胞中CAR和CD46的表达水平；分别以Ad5 TRAIL及Ad5F35 TRAIL重组腺病毒按MOI 10和50感染上述细胞，48 h后Annexin V FITC双标法流式细胞术检测细胞的早期凋亡。结果：A549、Z793、QG56和NCI H520 4株肺癌细胞中，CD46的表达均明显高于CAR表达。Z793、QG56细胞对Ad5 TRAIL和Ad5F35 TRAIL的作用较敏感，MOI=10感染后凋亡率分别为（11.76±2.10）%、（15.96±2.89）%和（6.05±1 58）%、（ 10.11± 1.26）%，显著高于对照组\[（2.33±0.37）%和(5.95±1.89）%， P <0.05\]；MOI=50感染时NCI H520细胞凋亡率分别为（12.89±3.2）%和（9.08±1.35）%，与对照组（7.04±2.17）%相比差异无统计学意义（ P >0.05）；Ad5 TRAIL和Ad5F35 TRAIL均不能诱导A549细胞凋亡。10例原代肺癌细胞CD46表达也明显较CAR高；Ad5 TRAIL或Ad5F35 TRAIL 感染后，5例的原代肺癌细胞检测到凋亡；与Ad5 TRAIL相比，Ad5F35 TRAIL诱导的凋亡率更高。结论：两种TRAIL重组腺病毒对非小细胞肺癌细胞均有凋亡诱导作用，Ad5F35 TRAIL的作用强于Ad5 TRAIL，更适合于非小细胞肺癌的基因治疗。

关键词：非小细胞肺癌 肿瘤坏死因子受体相关凋亡诱导配体 腺病毒 凋亡 柯萨奇腺病毒受体（CAR) CD46

CAR or CD46 dependent TRAIL adenoviral vector induced apoptosis in lung cancer cells Download Fulltext

MA Ling-di WANG Yong NI Cheng WANG Shi-zhong BAO Yong yi GUAN Nai-fu ZHANG Ke Leif G. Salford FAN Xiao long

Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;Laboratory Center, Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou 213003,China;The Rausing Laboratory, Lund University, SE 22184 Lund, Sweden;The Rausing Laboratory, Lund University, SE 22184 Lund, Sweden

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Abstract:

Objective:To observe the effects of recombinant adenovirus TRAIL (Ad5 TRAIL & Ad5F35 TRAIL) on apoptosis of non small cell lung (NSCLC) cells, so as to assess the value of Ad TRAIL in gene therapy of NSCLC. :Methods: :CAR and CD46 expression levels in lung cancer cell lines (A549, Z793, QG56 and NCI H520) and the primary lung cancer cells from samples of 10 NSCLC patients were assayed by flow cytometry analysis. The lung cancer cell lines and primary lung cancer cells were infected with Ad5 TRAIL & Ad5F35 TRAIL adenoviral vectors at MOI 10 or 50, respectively; the percentage of apoptosis cells labeled by Annexin V FITC in different cells were measured by flow cytometry 48 h after transfection. :Results:: The expression of CD46 were higher than that of CAR in all the lung cancer lines (A549, Z793, QG56 and NCI H520) and the primary lung cancer cells. Significant apoptosis was observed in Z793 and QG56 cells transfected with Ad5 TRAIL or Ad5F35 TRAIL at MOI 10, with the apoptosis rate being (1.76±2.10)%（Ad5 TRAIL）, (15.96±2.89)%（Ad5F35 TRAIL）and (6.05±1.58)%（Ad5 TRAIL）,(10.11±1.26)%（Ad5F35 TRAIL）, respectively, compared to no adenovirus transfected cells （\[2.33±0.37\]% and \[5.95±1.89\]%, respectively, P <0.05）. Less than 10% of apoptosis cells were detected in NCI H520 cells transfected with Ad5 or Ad5F35 TRAIL at MOI 50 (\[12.89±3.2\]% for Ad5 TRAIL and \[9.08±1.35\]% for Ad5F35 TRAIL, respectively）compared to no adenovirus transfected cells (\[7.04±2.17\]%, P> 0.05）. Moreover, apoptosis induced by Ad5 or Ad5F35 TRAIL transfection in A549 cells was not detected both at MOI 10 and 50. About half of the primary lung cancer cells from 10 patients induced apoptosis after transfected with Ad5 TRAIL or Ad5F35 TRAIL vector. A higher percentage of apoptotic cells were found in Ad5F35 TRAIL group than those in Ad5 TRAIL and control groups. :Conclusion: :Ad5 TRAIL can induce apoptosis of NSCLC cells in vitro, and Ad5F35 TRAIL is more potent than Ad5 TRAIL, so Ad5F35 TRAIL is more suitable for gene therapy of NSCLC.

Keywords:TNF recepter related apoptosis inducing ligand (TRAIL) adenovirus apoptosis coxsackie adenovirus receptor(CAR) CD46 non small cell lung cancer

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