182~186.沉默HuR的表达增加人乳腺癌耐药MCF-7/Adr细胞对多柔比星的敏感性[J].楚慧丽,王俊,朱忠鹏,郭燕,王宝成,毕经旺,李锴男,梁秀菊.中国肿瘤生物治疗杂志,2013,20(2)

沉默HuR的表达增加人乳腺癌耐药MCF-7/Adr细胞对多柔比星的敏感性 点此下载全文

楚慧丽 王俊 朱忠鹏 郭燕 王宝成 毕经旺 李锴男 梁秀菊

中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;山东省军区 门诊部，山东 济南 250013;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031;中国人民解放军济南军区总医院 肿瘤科，山东 济南 250031

基金项目：国家自然科学基金资助项目（No. 30901788, No. 81272619），山东省自然科学基金资助项目（No. ZR2010HQ038, No. ZR2010HM059）

DOI：10.3872/j.issn.1007-385X.2013.02.009

摘要：

目的：研究RNA干扰人抗原R（human antigen R，HuR）基因的表达对人乳腺癌耐药细胞株MCF-7/Adr对多柔比星（doxorubicin）敏感性的影响。 方法：构建靶向 HuR基因 的shRNA表达质粒（pGenesil-siHuR），稳定转染至MCF-7/Adr细胞，real-time PCR检测细胞中 MDR1 mRNA的表达，Western blotting检测MCF-7/Adr细胞中由 MDR1 基因编码的P糖蛋白（P-glycoprotein,P-gp）的表达，MTT法检测pGenesil-siHuR 转染后MCF-7/Adr细胞在多柔比星作用后的存活率和IC 50，流式细胞术检测MCF-7/Adr细胞的凋亡率。 结果： 与未转染的MCF-7/Adr细胞比较，pGenesil-siHuR质粒转染MCF-7/Adr细胞中 MDR1 mRNA的表达水平明显减低\[（0 184±0.029） vs （1.203±0.026），P<0.01\]，P-gp表达水平明显降低。pGenesil-siHuR质粒转染MCF-7/Adr细胞后，MCF-7/Adr细胞对多柔比星的IC 50从未转染的(148.2±2.3）nmol/L降至(42.9±0.4）nmol/L；经多柔比星处理后，pGenesil-siHuR质粒转染组MCF-7/Adr细胞的凋亡率明显上升\[（34.6±1.1）% vs （1.1±0.2）%，P<0 01\]。 结论： RNA干扰HuR的表达能抑制 MDR1基因 的表达，增加耐药乳腺癌MCF-7/Adr细胞对多柔比星的敏感性。

关键词：人抗原R基因 乳腺癌 MCF-7/Adr细胞 多药耐药 多柔比星 RNA干扰

Silencing HuR expression increases sensitivity of multidrug-resistant human breast cancer MCF-7/Adr cells to doxorubicin Download Fulltext

Chu Huili Wang Jun Zhu Zhongpeng Guo Yan Wang Baocheng Bi Jingwang Li Kainan Liang Xiuju

Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China;Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China;Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China;Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China;Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China;Department of Oncology, General Hospital, Jinan Military Command of People’s Liberation Army, Ji′nan 250031, Shandong, China

Fund Project:Project supported by the National Natural Science Foundation of China (No. 30901788, No. 81272619) , and the Natural Science Foundation of Shandong Province (No. ZR2010HQ038, No. ZR2010HM059)

Abstract:

Objective: To investigate the effect of interference of human antigen R (HuR) expression on sensitivity of human multidrug-resistant human breast cancer MCF-7/Adr cell line to Doxorubicn. Methods: The shRNA expression vector targeting HuR gene (pGenesil-siHuR) has been constructed and stably transfected into human breast cancer MCF-7/Adr cell line. The expression level of MDR1 mRNA in MCF-7/Adr cells was assayed by real-time PCR. The P-gp protein (encoded by the MDR1 gene) expression were determined by Western blotting. The survival rate and IC 50 of MCF-7/Adr cells to doxorubicin after pGenesil-siHuR transfection were evaluated by MTT method. The apoptosis rate of MCF-7/Adr cells was detected by flow cytometry. Results: Compared with untransfected MCF-7/Adr cells, the MDR1 mRNA（\[0.184±0.029\] vs \[1.203±0.026\], P<0.01）and P-gp protein expressions（\[0.314±0.011\] vs \[0.796±0 007\], P<0.01）were significantly reduced in pGenesil-siHuR transfected MCF-7/Adr cells (P<0.01). The IC 50 of MCF-7/Adr cells to doxorubicin decreased from (148.2±2.3) nmol/L to (42.9±0.4) nmol/L after pGenesil-siHuR transfection. Compared with untransfected MCF-7/Adr cells, the ratio of cell apoptosis was significantly increased in pGenesil-siHuR transfected MCF-7/Adr cells （\[34.6±1.1\]% vs \[1.1±0.2\]%, P<0.01）after the treatment with doxorubicin. Conclusion: RNA interference of HuR can inhibit the expression of MDR1 gene and increase the sensitivity of multidrug-resistant breast cancer cells to doxorubicin.

Keywords:human antigen R gene breast cancer MCF-7/Adr cell multidrug-resistant doxorubicin RNA interference